Current Indications for Transcatheter Aortic Valve Implantation

Ibrahim Akin, Stephan Kische, Henrik Schneider, Tim C. Rehders, Christoph A. Nienaber and Hüseyin Ince
University of Rostock
Germany

1. Introduction

Rising life expectancy results in an increase of degenerative and neoplastic diseases. Population-based observational studies report that 1% to 2% of patients older than 65 years have moderate-to-severe aortic stenosis (AS) (Nkomo et al., 2006). Surgical aortic valve replacement (AVR) dates back to 1960 and is currently the only treatment option for severe AS that has been shown to improve survival, regardless of age (Kvidal et al., 2000). In the ideal candidate, surgical AVR has an estimated operative mortality of 4% (Kvidal et al., 2000). Unfortunately, up to one-third of patients with severe AS are ineligible for corrective valve surgery, either because of advanced age or the presence of multiple comorbidities (Iung et al., 2005). Current treatment options for those patients not offered surgery include medical treatment or percutaneous balloon aortic valvuloplasty, although neither has been

Fig. 1. Survival of medically treated symptomatic AS (Ross J Jr. & Braunwald E, 1965)
shown to reduce mortality. Medically treated patients with symptomatic AS have 1- and 5-year survival of 60% and 32%, respectively (Varadarajan et al., 2006) (Figure 1). With the introduction of percutaneous aortic valve implantation in 2002, there seems to be an alternative for these patients.

2. Selection of patient

Due to the existence of tried and tested surgical AVR with good long-term results, the selection of patients for transcatheter aortic valve implantation (TAVI), which should done in a multidisciplinary consultation between cardiologists, surgeons, imaging specialists, and anesthesiologists, involves several critical steps (Vahanian et al., 2008). Candidates considered for TAVI must have severe symptomatic AS in addition to a formal contraindication to surgery or other characteristics that would limit their surgical candidacy because of excessive mortality or morbidity (Figure 2). The procedure should be offered to patients who have a potential for functional improvement after valve replacement. It is not recommended for patients who simply refuse surgery on the basis of personal preference.

Fig. 2. Algorithm to determine the treatment options of patients with severe AS. (AVA: aortic valve area; TAVI: transcatheter aortic valve implantation)
3. Confirming the severity of aortic stenosis

Actually, TAVI is indicated only for patients with calcified pure or predominant symptomatic AS. The different imaging modalities can assist in the selection process by providing important information on the aortic valve, coronary arteries, and vascular structures. First, the severity of AS should be assessed. Both transthoracic (TTE) and transesophageal (TEE) Doppler echocardiography are the preferred tools (Figure 3).

![Fig. 3. TTE in the assessment of severe AS](image)

In addition, the exact anatomy of the aortic valve should be assessed. Echocardiography, multislice CT (MSCT), and magnetic resonance imaging (MRI) can all help to distinguish between a bicuspid and a tricuspid aortic valve. It is important to point out that implantation of available percutaneous prostheses is contraindicated in the case of a bicuspid aortic valve, because of the risk of incomplete deployment, significant paravalvular regurgitation, and displacement of the prosthesis (Vahanian et al., 2008; Zegdi et al., 2008) (Figure 4).

A severely calcified aortic valve may result in the inability to cross the native valve with the catheter. Bulky leaflets and calcifications on the free edge of the leaflets may increase the risk of occlusion of the coronary ostia during aortic valve implantation. Therefore, the extent and exact location of calcifications should be carefully assessed before the implantation procedure.

Assessing coronary anatomy is also important in the selection process. Conventional coronary angiography, which remains the “gold standard”, should be done to exclude the presence of significant coronary artery disease (Figure 5).

4. Analysis of surgical risk and evaluation of life expectancy and quality of life

The precise evaluation of surgical risk in a specific patient is not easy and involves an attempt at individualization based on statistical data from databases containing a large number of procedures. The most accepted and validated algorithms that are widely available today are the EuroSCORE, the STS (Society of Thoracic Score) score, and the Parsonnet score. These algorithms predict the surgical risk by assigning weight to various factors that affect the clinical result, but it is clear that they can underestimate or overestimate the risk in certain groups of patients who are not represented satisfactorily in the population used to generate the algorithm (Roques et al., 2001). There is some evidence
in the literature of the incorrect prediction of aortic AVR outcome using the EuroSCORE model (Grossi et al., 2008). The key element for establishing whether patients are at high risk for surgery is multidisciplinary clinical judgment, which should be used in association with a more quantitative assessment, based on the combination of several scores (for example, expected mortality >20% with the EuroSCORE and >10% with STS score). This approach allows the team to take into account risk factors that are not covered in scores but often seen in practice, such as chest radiation, previous aortocoronary bypass with patent grafts, porcelain aorta, liver cirrhosis.

Fig. 4. ECG-gated CT-scan in a patient with severe aortic valve stenosis (the upper right panel shows the isolated calcification of the tricuspid aortic valve)

Fig. 5. Invasive diagnostic prior TAVI, including aortography and access vessels as well as transvalvular gradient

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5. Assessment of feasibility and exclusion of contraindications for TAVI

After criteria of severe symptomatic aortic valve stenosis and high surgical risk are evaluated, the technical evaluation of the patient’s suitability for the percutaneous implantation technique begins (Table 1).

**Indication for Transcatheter aortic valve implantation**

- Severe aortic stenosis (AVA: $<1cm^2$, mean gradient $>40mmHg$, severe symptoms)
- Contraindication for surgical valve replacement

**Contraindication for Transcatheter aortic valve implantation**

- Mild to moderate aortic stenosis
- Asymptomatic patients
- Life expectancy <1 year
- Surgical aortic valve replacement possible, but patient refused
- Aortic anulus $<18$ or $>25mm$ (balloon-expandable) and $<20$ or $>27mm$ (self-expandable)
- Bicuspid aortic valve
- Asymmetric heavy valvular calcification
- Aortic root $>45mm$ at the aortotubular junction
- Presence of left ventricular apical thrombus

**Contraindication for transfemoral approach**

- Severe calcification, tortuosity, small diameter of the iliac arteries
- Previous aortofemoral bypass
- Severe angulation, severe atheroma of the aorta
- Coarctation of the aorta
- Aneurysm of the aorta with protruding mural thrombus

**Contraindication for transapical approach**

- Previous surgery of the left ventricle using a patch
- Calcified pericardium
- Severe respiratory insufficiency
- Non-reachable left ventricular apex

Table 1. Actually proposed indications and contraindications for TAVI
The two most basic parameters are the suitability of the peripheral arteries and the size of the aortic valve annulus. Contrast angiography is needed to assess the former, while the latter requires an initial assessment of the diameter of the aortic annulus on a TTE. In general terms, a large artery with dominant elastic elements should have a diameter up to 1 mm smaller than the external diameter of the sheath that has to be introduced for the valve implantation. Thus, current systems with an external sheath diameter of 28 F (SAPIEN 26 mm, Edwards Lifescience LLC, Irvine, CA), 25 F (SAPIEN 23 mm, Edwards) and 22 F (CoreValve, Medtronic, Inc., Minneapolis, MN) require minimum diameters of 8, 7, and 6 mm, respectively. Apart from the minimum diameter, the existence of significant vessel tortuosity (>90°), especially when combined with wall calcifications, makes advancing the large sheath problematic, with a high risk of vascular complications that could potentially affect the final outcome. In addition, the existence of extensive circumferential calcifications limits the elastic dilation of the artery; thus, the minimum diameters referred to above are underestimated. Patients who do not meet the criteria of suitable peripheral arterial access may still be candidates for transapical implantation. For the assessment of aortic annulus diameter, we should keep in mind that TTE underestimates its size by a mean of 1.4 mm compared with TEE (Babaliaros et al., 2008; Vahanian et al., 2008), while the latter method also underestimates the size by 1.2 mm compared with intraoperative measurement (Babaliaros et al., 2008). Therefore, in order to avoid undesirable and often catastrophic displacement of the prosthesis, there should be a margin of at least 1-2 mm between the diameter of the valve and the size of the aortic annulus estimated using TEE, so that the former may be successfully and safely anchored within the latter. Computed tomography scan aortography and angiography of the ascending aorta are the most appropriate examinations for investigating these aspects. Those examinations will also be used for the measurement of the dimensions of the ascending aorta and the aortic arch, which are essential for checking eligibility for the CoreValve (the most important being the diameter of the ascending aorta, which should be <4.3 cm) (Figure 6).

Fig. 6. ECG-gated CT-scan of a patient with severe aortic valve stenosis and porcelain aorta after radiation exposure
The anatomy of the thoracic aorta (any chance of porcelain aorta) and the abdominal aorta should be studied by some imaging method for the existence of extensive atheromatosis, mural thrombi and aneurysm.

Fig. 7. Three-dimensional reconstruction of contrast-enhanced CT angiography to assess morphology of femoral arteries (left) and centerline stretched view (right)

6. Different transcatheter aortic valves

On the basis of first results from clinical trials, CoreValve Revalving System and Edwards Lifescience SAPIEN obtained CE mark approval in 2007 with the specification that these valves are intended for patients with a high or prohibitive risk for surgical valve replacement or who cannot undergo AVR. The first generation balloon-expandable valve was entitled Cribier-Edwards valve (Edwards Lifesciences), whereas at present the Edwards SAPIEN valve (Edwards) is commercially available (Figure 8). The Edwards Lifesciences SAPIEN THV device is a balloon-expandable valve. It consists of bovine pericardium that is firmly mounted within a tubular, slotted, stainless steel balloon-expandable stent. Two

Fig. 8. Profile of the CoreValve Revaving System (A) and Edwards SAPIEN Transcatheter Heart Valve (B)
valve sizes have been developed (23mm and 26mm). At present, available prosthesis sizes are 23 and 26 mm for aortic annulus diameters between 18–22 mm and 21–25 mm, respectively. The CoreValve Revalving device is a self-expanding frame-valve prosthesis (Figure 2). It consists of a porcine pericardial tissue valve that is mounted and sutured in a multilevel self-expanding nitinol frame. It is available in 26 and 29 mm sizes. The device has a broader upper segment (outflow aspect), which yields proper orientation to the blood flow. The first-generation valve used bovine pericardial tissue and was constrained within a 25 French (F) delivery catheter. The second-generation valve was built with porcine pericardial tissue within a 21 F catheter to allow access through smaller-diameter vascular beds. The third-generation of the device features a catheter with a valve delivery sheath size of 18 F and a follow-on shaft of 12 F.

Newer devices that have first-in-man application include Paniagua (Endoluminal Technology Research, Miami, FL), Enable (ATS, Minneapolis, MN), AoTx (Hansen Medical, Mountain View, CA), Perceval (Sorin Group, Arvada, CO), Jena (JenaValve Technology, Wilmington, DE), Lotus Valve (Sadra Medical, Campbell, CA), and Direct Flow percutaneous aortic valve (Direct Flow Medical, Inc., Santa Rosa, CA). TAVI represents a unique challenge for anesthesiologists. As with other invasive procedures, a careful preoperative assessment, appropriate intraoperative monitoring and imaging, meticulous management of hemodynamics, and early treatment of expected side effects and complications is of utmost importance. An unexpected decrease or increase in systemic vascular resistance resulting in decreased coronary perfusion pressure or acute heart failure by elevated left ventricular end-diastolic pressure should be avoided by maintaining a normotensive blood pressure and heart rate between 60 bpm and 100 bpm. The choice of anesthetic technique, either local anesthesia with mild sedation promoting spontaneous respiration, deep intravenous sedation with insertion of a laryngeal mask, or general anesthesia, varies among centers and is probably not associated with a significant difference in outcome. Post valvuloplasty and implantation, which were done under rapid right ventricular pacing due to reduce left ventricular ejection and cardiac motion, may require some additional inotropic support. Tracheal extubation can usually be done at the end of the procedure. Close postoperative monitoring is necessary, and admission to an intensive care unit is required. However, at present a retrograde approach through the femoral artery is used. During the procedure, a balloon valvuloplasty is first done to facilitate passage of the native aortic valve. During rapid right ventricular pacing, the prosthesis is positioned and deployed under fluoroscopy and echocardiographic guidance. Alternatively, in patients with difficult vascular access because of extensive calcifications or tortuosity of the femoral artery or aorta, a transapical approach can be used. After a partial thoracotomy, direct puncture of the apical portion of the left ventricular free wall is done to gain catheter access to the left ventricle and aortic valve. The prosthesis is subsequently positioned and deployed, similar to the antegrade approach.

7. Implantation approaches

With regard to the delivery systems and their introduction into ascending aorta, two specific pathways have been explored so far: the antegrade pathway, which uses direct transapical access, and the retrograde pathway, which uses either transfemoral or trans-subclavian or trans-axillary access (De Robertis et al, 2009).
7.1 The transapical approach

The main advantages of using transapical procedures are: [1] the feasibility does not rely on the absence of a concomitant peripheral vascular disease or previous aortic surgery; [2] the delivery system seems to be more “steady” and the procedure itself more “straightforward”; and [3] this access potentially reduces the risk of calcium dislodgement due to the passage of a stiff transfemoral device into a diseased aortic arch. A transapical approach can be used in the operating room, in a hybrid room, or in a catheterization laboratory with a patient under general anesthesia. Regardless of where the transapical approach is done, it is a prerequisite that high-quality fluoroscopic imaging must be guaranteed. Apical bleeding is very rare, mostly related to patient tissue fragility or to the team learning curve, and represents the most dangerous complication related to transapical access itself. In transapical TAVI, the cardiac apex is prepared through a small left anterolateral mini-thoracotomy using a purse-string or a crossing suture reinforced by pledgets and, after the procedure, a chest tube is routinely inserted into the left pleura with pain releasers injected in the intercostal tissue (Figure 9).

Fig. 9. TAVI using the transapical approach

7.2 The transfemoral approach

The transfemoral approach is used mostly in cardiac catheterization laboratory or a hybrid room. One of the main advantages of this technique is that it allows fully percutaneous implantation in conscious patients, as long as the peripheral vessels are of an adequate caliber (more than 6mm diameter), there are no very tortuous vessels, and vascular closure devices are available (Figure 10). Alternatively, the standard technique requires surgical preparation of the common femoral artery under local or general anesthesia. Major and minor postoperative vascular complications have been reported quite often in recent series (Grube et al., 2006; Eltchaninoff et al., 2011) and some critical events (vessel dissections, ruptures or avulsions) might be catastrophic when not promptly and adequately treated.

7.3 The trans-subclavian approach

Trans-subclavian access is an alternative retrograde pathway that has been recently explored. It requires a surgical exposure of the left subclavian artery and an adequate minimal vessel inner diameter for 18F delivery systems (Figure 11). There are some advantages in using this approach: firstly, the distance between the site of introduction and
the aortic valve is short, compared with the transfemoral option, and it results in a steadier pathway. Secondly, as long as the subclavian artery is intact, the trans-subclavian procedure can be done in case of a concomitant vascular disease involving the abdominal aorta or the legs, and it does not require a thoracotomy. Unfortunately, the presence of a patent internal mammary artery, such as a diseased subclavian artery, in redo coronary surgery contraindicates this approach. However, at this moment, this interesting approach remains “off-label” and is not yet formally recommended by the industry.

Fig. 10. TAVI using the transfemoral approach

7.4 The trans-aortic approach

In case of severe vascular disease and a concomitant contraindication to transapical procedures, an alternative, interesting, retrograde approach has been proposed: through an upper “J-shape” mini-sternotomy, the guidewire and the delivery system are inserted, retrogradely, into the ascending aorta and are secured with a double-string suture. TAVI is then done as a transfemoral procedure. The presence of “porcelain” aorta and the risk of postoperative massive bleeding limit this approach to selected patients.
8. Results from the literature

8.1 Cribier-Edwards valve

Cribier et al. (2002) did the first human implantation in 2002. The Edwards SAPIEN valve was approved for use in the European Union in November 2007 (for the transfemoral approach) and in January 2008 (for transapical delivery). In the Initial Registry of EndoVascular Implantation of Valves in Europe (I-REVIVE) trial, followed by the Registry of Endovascular Critical Aortic Stenosis Treatment (RECAST) trial, a total of 36 patients (mean (SD) EuroSCORE 12 (2)) were included (Cribier et al., 2004). Twenty-seven patients underwent successful percutaneous aortic valve implantation (23 antegrade, 4 retrograde). The 30-day mortality was 22% (6 of 27 patients), and the mean AVA increased from 0.60 ± 0.11cm² to 1.70 ± 0.10cm² (p<0.001). Importantly, this improvement in AVA was maintained up to 24 months follow-up (Cribier et al., 2006). Since these first trials, the Cribier-Edwards prosthesis and the Edwards SAPIEN prosthesis have been used in numerous studies. Overall, acute procedural success is achieved in 75–100% of the procedures, and 30-day mortality ranges between 8–50% in the published studies. Using the transapical technique and the Sapien valve, Walther et al. (2007) has reported their initial multicenter results of 59 consecutive patients, which is the largest feasibility study published thus far. Procedural success using the transapical technique was achieved in 53 patients. Thirty-day mortality was 13.6% and none of these were thought to be valve related as there was good valve function at autopsy. The overall procedural success of 1038 SAPIEN implants from 32 centers within the European SOURCE registry was 93.8%. The 30-day survival within SOURCE was 93.7% (transfemoral) and 89.7% (transapical) (Thomas, 2010). The 1-year survival of the cohort was 81.1% (transfemoral) and 72.1% (transapical), respectively. In cohort B of the PARTNER randomized trial, 179 patients receiving transfemoral SAPIEN aortic valve with 179 patients receiving standard medical therapy (including balloon aortic valvuloplasty), confirmed the superiority of transfemoral TAVI with regard to overall survival and cardiac functional status (Leon et al., 2010). The Kaplan-Meier 1-year mortality from any cause was 30.7% (TAVI) versus 50.7% (standard medical therapy), corresponding
to a 0.55 hazard ratio with TAVI (p<0.001). The fraction of surviving patients at 1-year, in New York Heart Association functional class III-IV, was lower in the TAVI group (25.2% versus 58%; p<0.001). Nevertheless, the TAVI group had a higher 30-day incidence of major stroke (5.0% versus 1.1%; p=0.06) and major vascular complications (16.2% versus 1.1%; p<0.001). Early and 1-year outcomes from the REVIVAL trial, which consisted of 55 patients with a mean AVA of 0.57±0.14cm² and a mean logistic EuroSCORE of 33.5±17%, have been reported (Kodali et al., 2011). TAVI was successful in 87%. Mean echocardiographic AVA improved from 0.56±14 to 1.6±0.48cm² after the procedure (p<0.0001). Thirty-day all-cause mortality and major adverse cardiac events (MACE) were 7.3% and 20%, respectively. These rates increased to 23.6% and 32.7%, respectively, at 1 year, with most late events related to underlying comorbidities. The mean NYHA functional class improved from 3.22±0.66 at baseline to 1.50±0.85 at 1-year follow-up (p<0.001).

8.2 CoreValve ReValving
Since the first implantation of the CoreValve prosthesis in a patient in 2005 (Grube et al., 2005), a large number of patients have been treated with this device. The feasibility and safety of this valve was studied in a prospective, multicenter trial (Grube et al., 2006). A total of 25 symptomatic patients with an AVA < 1cm² were enrolled in the study. The device was successfully implanted using the retrograde technique in 22 of 25 patients. Procedural success and aortic mean pressure gradients were markedly improved immediately following implantations with pre-procedure gradients 44.24 ± 10.79 mmHg to 12.38 ± 3.03 mmHg post-procedure, and were about the same at 30-day follow-up (11.82 ± 3.42 mm Hg). NYHA functional class improved by 1 to 2 grades in all patients. MACE, defined as death from any cause, major arrhythmia, myocardial infarction, cardiac tamponade, stroke, urgent or emergent conversion to surgery or balloon valvuloplasty, emergent percutaneous coronary intervention, cardiogenic shock, endocarditis, or aortic dissection, occurred in 8 of the 25 hospitalized patients. Recently, Grube et al. (2008) reported the results with the three different generations of the CoreValve Revalving system in a non-randomized, prospective study of 136 patients. Ten patients were treated with first-generation devices, 24 patients with second-generation, and 102 patients with third-generation devices. At baseline, mean AVA was 0.67cm² and mean logistic EuroSCORE was 23.1% in the overall study population. With the new-generation devices, the overall procedural success rate significantly increased from 70.0% and 70.8% to 91.2% for the first-, second-, and third-generation prostheses, respectively (p = 0.003). Interestingly, using newer devices, periprocedural mortality decreased from 10% (first-generation) to 8.3% (second-generation) to 0% (third-generation). Overall 30-day mortality for the three generations was 40%, 8.3% and 10.8%, respectively. Pooled data demonstrated a significant improvement in mean NYHA functional class (from 3.3 to 1.7, p<0.001), without a difference between the three generations. Importantly, NYHA functional class and mean pressure gradient remained stable up to 12 months follow-up in all three generations. In addition, the results of a multicenter registry with the third-generation CoreValve Revalving system have recently been reported (Piazza et al., 2008). A total of 646 patients from 51 centers were included in the registry. It was a high-risk elderly population (mean age: 81 years) with a poor functional class (85% of the patients in NYHA class III or IV), and a high logistic EuroSCORE (mean: 23.1%). Procedural success was achieved in 628 of the 646 patients (97.2%). All-cause 30-day mortality was 8%, and the
combined end point of procedural related death, stroke, or myocardial infarction was reached in 60 patients (9.3%). After successful implantation, mean pressure gradient decreased from 49 mmHg to 3 mmHg (Piazza et al., 2008). The FRANCE real-world registry of 244 consecutive high-risk patients with symptomatic severe AS, enrolled from 16 centers over a period of 5 months in 2009, reported 98.3% procedural success for both Edwards SAPIEN and Medtronic CoreValve (66% transfemoral, 5% subclavian, and 29% transapical) prostheses (Eltchaninoff et al., 2011). The 30-day mortality was 12.7%, and, at 1 month, 88% of patients were in NYHA class I-II. Buellesfeld et al. (2011) reported on a 2-year follow-up of 126 patients who underwent TAVI. Thirty-day all-cause mortality was 15.2%. At 2-years, all-cause mortality was 38.1%, with a significant difference between the moderate-risk group and the combined high-risk groups (27.8% versus 45.8%; p=0.04). This difference was attributable to an increased risk of noncardiac mortality in high-risk groups. Hemodynamic results remained unchanged during follow-up (mean gradient: 8.5±2.5mmHg at 30 days and 9.0±3.5mmHg at 2 years) without any incidence of structural valve deterioration.

Fig. 12. TAVI in a patient with a history of AVR

Fig. 13. TAVI in a patient with a history of mitral valve replacement

The larger CoreValve prostheses (26 and 29 mm) were the only device for annulus between 26 and 27 mm, before the currently available 29-mm SAPIEN XT valve for transapical implantation. The CoreValve prosthesis had previously been the only device suitable for transarterial implant in patients with limited iliofemoral artery access, but this has changed
with the SAPIEN NovaFlex delivery system. The growing experience with the subclavian artery approach, however, allows the CoreValve prosthesis to be implanted in patients with unusable iliofemoral arteries. Because of these results, the indications for TAVI expanded (e.g. in patients with porcelain aorta, with previous cardiac surgery, etc.) (Wenaweser et al., 2007) (Figure 12,13).

9. Conclusion

Transcatheter aortic valve implantation was developed to provide an alternative and less invasive method of treating aortic valve stenosis. Actually, it has been proved that the method is feasible, with results that have been reproduced by many physicians in many centers (approximately 10,000 implantations to date). Today there are at least 10 new transcatheter aortic valves that have had their first implantation in humans, many more that have reached the level of animal experiments, and even more that are still in the initial design stage. As a new treatment tool, it has to be evaluated in randomized controlled trials with long-term follow-up in order to assess safety and efficacy. Therefore, TAVI should be restricted to a limited number of high-volume centers, that have both cardiology and cardiac surgery departments as well as expertise in structural heart disease intervention and high-risk valvular surgery. Because of excellent results with surgical valve replacement, patient selection, which should be done in multidisciplinary conferences, is of utmost importance. Like other interventional procedures, there is a learning curve with significant improvements in the success rate and the clinical results after the first 25 procedures, which implies that the TAVI procedure should initially be done by and thereafter supervised by a special team (Walther et al., 2009; Webb et al., 2007). In addition to patient selection and intervention of TAVI, a close follow-up with assessment of clinical and objective parameters is mandatory for defining the indications of this technique.

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Much has evolved in the field of aortic valve disease because of the increase in knowledge in the last decade, especially in the area of its management. This book "Aortic Valve" is comprised of 18 chapters covering basic science, general consideration of aortic valve disease, infective endocarditis, aortic sclerosis and aortic stenosis, bioprosthetic valve, transcatheter aortic valve implantation and a special section on congenital anomalies of the aortic valve. We hope this book will be particularly useful to cardiologists and cardiovascular surgeons and trainees. We also believe that this book will be a valuable resource for radiologists, pathologists, cardiovascular anesthesiologists, and other healthcare professionals who have a special interest in treating patients with aortic valve disease. We are certain that information in this book will help to provide virtually most new areas of aortic valve disease that will be employed in the current era.

How to reference
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