Anatomic Suitability for Present and Next Generation Transcatheter Aortic Valve Prostheses

Evidence for a Complementary Multidevice Approach to Treatment

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Objectives This study sought to assess the proportion of patients anatomically suitable for transcatheter aortic valve implantation by multiple access approaches.

Background The devices currently in mainstream use for transcatheter treatment of severe aortic stenosis are those of Edwards (Edwards Lifesciences, Nyon, Switzerland) and Medtronic CoreValve (M-C) (Luxembourg City, Luxembourg). The range of patients that these can presently treat requires elucidation to guide the necessary evolution of these technologies and increase their scope of therapy.

Methods A consecutive series of patients were assessed with transthoracic or transesophageal echocardiography and invasive angiography to assess anatomical suitability by different approaches. The transfemoral access requirements for Edwards and M-C (Edwards currently 22- and 24-F, soon to be 18- and 19-F; M-C 18-F) as well as the aortic valve annular criteria (18 to 25 mm and 20 to 27 mm, respectively) were incorporated in this assessment. Patients unsuitable for the transfemoral approach were considered for Edwards transapical and M-C transaxillary and direct ascending aortic access. Patients suitable for these devices and access approaches were identified.

Results Data were analyzed for 100 consecutive patients. Edwards suitability was 28% for Edwards-Sapien transfemoral, 78% for Edwards Novaflex transfemoral, and 88% for Edwards-Sapien transapical. Medtronic CoreValve suitability was 84% for transfemoral and 89% using additional transaxillary and direct aortic approaches. Of the 12 patients unsuitable for Edwards-based procedures, 8 were suitable for M-C. Of the 11 patients unsuitable for M-C–based techniques, 8 were suitable for Edwards. Only 3% were anatomically unsuitable for all approaches.

Conclusions In this series, 97% of patients were anatomically suitable for a complementary approach to treatment. (J Am Coll Cardiol Intv 2010;3:859–66) © 2010 by the American College of Cardiology Foundation
Transcatheter aortic valve implantation (TAVI) has achieved great success in treating high-risk and inoperable patients with severe aortic stenosis (1–8). The 2 devices in mainstream use (post-CE mark) in Europe are the Medtronic CoreValve (Luxembourg City, Luxembourg) (3) and the Edwards Sapien (Edwards Lifesciences, Nyon, Switzerland) (6) devices, accounting for over 12,000 implants to-date worldwide. However, anatomical constraints remain, in particular with peripheral arterial access for transfemoral approaches and aortic valve annular dimensions for all approaches. The impact of these constraints on the treatment offered to a range of patients is unknown; the magnitude and nature of the impact may guide further evolution of technology, allowing physicians to offer safe therapy to the wider pool of patients with aortic stenosis who are not treated (9). In a 2-center series of consecutive patients assessed for TAVI, we therefore determined the proportion of patients anatomically suitable for treatment by the multiple approaches available. We evaluated this using selection criteria for present devices and those for imminent next-generation devices. We hypothesized that a greater proportion of patients could be treated if both device types and all approaches were available in the selection process.

**Abbreviations and Acronyms**

**TAVI** = transcatheter aortic valve implantation

**Methods**

**Patient assessment.** A consecutive series of 100 patients were assessed in 2 centers and data prospectively collected. All patients were considered at high or prohibitive risk of conventional surgery as assessed by a multidisciplinary team consisting in each center of at least 2 interventional cardiologists, 2 cardiothoracic surgeons, a cardiac anesthesiologist, and a cardiologist specializing in imaging. Our present selection algorithm is shown (Fig. 1). Transthoracic or transesophageal (in cases of suboptimal echogenicity) echocardiography was employed for annular measurements, with end-diastolic measurement from hinge point to hinge point in the parasternal or mid-esophageal long-axis views. Suitability by annular dimension was based on the criteria for each respective device. Invasive angiography and/or multislice computed tomography were used to measure minimal iliofemoral dimension from mid-femoral head proximally; a graduated pigtail was employed for calibration. The true minimum dimension was taken as the selection criteria for suitability; in patients with acceptably large common femoral arteries, dilation of iliac stenoses to gain vascular access was not permitted in the protocol. The proportion of patients suitable for each device by transfemoral approach was calculated.

**Edwards suitability.** The annular dimension criteria for Edwards Sapien device is 18 to 22 mm for the 23-mm device and 21 to 25 mm for the 26-mm device (10). The transfemoral access requirements for Edwards Sapien, with the Retroflex 3 system (Edwards Lifesciences), is a minimal iliofemoral dimension of at least 7 mm for the 22-F/23-mm device; and a minimal iliofemoral dimension at least 8 mm for the 24-F/26-mm device. An alternative access approach for the Edwards system is transapical, which obviates the need for large peripheries. It should be noted that the original PARTNER (Placement of AoRTic traNscathetER valves) trial (11) excluded patients with native aortic annulus size <16 mm or >24 mm on the baseline echocardiogram but this was estimated by the left ventricular outflow tract.

The imminent next-generation Edwards system (Edwards XT) with Novaflex delivery system is 18-F for the 23-mm device, requiring a minimal iliofemoral dimension of at least 6 mm and 19-F for the 26-mm device, requiring a minimal iliofemoral dimension of at least 6.5 mm (12). The proportion of patients from the series suitable for these devices and access approaches was determined.

**Medtronic CoreValve suitability.** The annular dimension requirement for Medtronic CoreValve is 20 to 23 mm for the 26-mm device and 23 to 27 mm for the 29-mm device (3). For transfemoral access, the device has 18-F requirements (minimal iliofemoral dimension at least 6 mm). An additional requirement is that the ascending aorta diameter 40 mm distal to the aortic annulus be <40 mm (for the smaller 26-mm inflow valve) and <43 mm (for the larger 29-mm inflow valve). Alternative approaches for the Medtronic CoreValve device are transaxillary (13,14) and direct access via the ascending aorta (15), which allow implantation in the setting of nonpermissive iliofemoral vessels. The proportion of patients from the series suitable for these approaches for the Medtronic CoreValve device was determined.

**Statistical analyses.** The range of patients suitable for a 2-device TAVI strategy was compared with that suitable for single-device approaches with Edwards and CoreValve, respectively, using McNemar paired nominal tests for individual patients in the consecutive series; the additional range of patients made suitable for TAVI with a 2-device approach by alternative access (transapical for Edwards and axillary/direct aortic access for CoreValve) was compared with that suitable for a 2-device transfemoral approach. Averages for continuous data are represented as the mean ± SD.

**Results**

Data were analyzed for 100 consecutive patients. Mean age was 80.9 ± 7.4 years and mean logistic EuroSCORE
The distribution of annular dimensions and minimum lumen diameter of the iliofemoral artery on the largest side are illustrated in Figures 2 and 3. Edwards Sapien suitability was 28% for the current transfemoral devices, 88% for the Edwards Sapien transapical device, and 78% for the Edwards XT Novaflex transfemoral device. Medtronic CoreValve suitability was 84% for transfemoral and 89% using additional transaxillary and direct aortic approaches. Notably, the increase in the upper limit of annular suitability from 24 to 25 mm for the Edwards Sapien system increased the suitability from 20% to 28% for the transfemoral approach and 74% to 88% for the transapical approach (Table 1).

Of the 12 patients unsuitable for Edwards-based procedures, 8 were suitable for Medtronic CoreValve. Of the 11 patients unsuitable for Medtronic CoreValve–based techniques, 8 were suitable for Edwards. Only 3% of the whole population was anatomically unsuitable for all approaches.

A 2-device strategy increased patients suitable for TAVI to 97% from 88% for Edwards-based approaches (p = 0.004) and from 89% for Medtronic CoreValve–based approaches (p = 0.008). There were 97% of patients suitable for TAVI by any approach with either device, compared with 92% of patients suitable for a multidevice transfemoral approach alone (p = 0.063). The 92% of patients suitable for a multiple device transfemoral approach was significantly greater than the 28% suitable for Edwards
Sapien transfemoral (p < 0.001), the 78% suitable for Edwards XT Novaflex transfemoral (p < 0.001) and the 84% suitable for the Medtronic CoreValve–based transfemoral (p = 0.008) approaches.

Outcomes in those undergoing TAVI. Of the 100 consecutive cases assessed, 52 have thus far undergone TAVI. These patients had a mean age of 82.6 ± 5.8 years and a mean logistic EuroSCORE of 21.1 ± 14.6. There was procedural failure in 2 cases (3.8%), post-procedural stroke in 1 (1.9%), and 30-day mortality in 4 (7.6%). Baseline aortic valve area was 0.72 ± 0.18 cm² and increased to 1.75 ± 0.43 cm² on pre-discharge echocardiogram. No significant post-procedural transvalvular aortic regurgitation was seen. Paravalvular aortic regurgitation of grade 2 or more was seen in 5 patients (9.6%); this was of grade 3 in 1 and there were no cases of grade 4 aortic regurgitation seen.

In 3 cases, TAVI was performed in cases anatomically unsuitable according to selection criteria. In 1 case, a CoreValve device was implanted despite a large proximal ascending thoracic aorta (47 mm) and was uncomplicated. In a further case, before the availability of the transapical and transaxillary approaches, a transfemoral CoreValve was implanted with a dottering maneuver despite sub-6-mm diffusely diseased and calcified iliofemoral vessels (Fig. 4A) and resulted in acute thrombosis (Fig. 4B) following partial arterial avulsion on sheath removal; there was no major bleeding and the thrombus resolved with heparinization without adverse sequelae. In the third case, a 23-mm transfemoral Edwards Sapien valve was implanted in a patient with a short segment proximal iliac stenosis (6.7 mm) whereas the remainder of the iliofemoral vasculature was appropriately sized; this was performed without complication.

Discussion

This study of consecutive patients referred for TAVI demonstrates that with a 2-device strategy, more patients are anatomically suitable for this therapy. This is because the principal limitation for Edwards Sapien (large annular dimension) differs from those for Medtronic CoreValve (small annulus dimension and large proximal ascending aortic dimension). Therefore, the use of both devices is
complementary and makes TAVI available for patients at either end of anatomical requirements.

It has been recently appreciated that measurements of the aortic annulus using transthoracic echocardiography, transesophageal echocardiography, and multislice computed tomography are similar but not identical, and the method used has important potential clinical implications for TAVI strategy (16). Some operators have used balloon aortic valvuloplasty to help determine appropriate transcatheter aortic valve size (17).

The selection constraints imposed by iliofemoral vessel size can be minimized by a transfemoral approach using both the Medtronic CoreValve 18-F system and the Edwards XT 18-F/19-F Novaflex delivery system. These

Table 1. Unsuitability for Different Devices and Approaches Currently Widely Available

<table>
<thead>
<tr>
<th>Reason Unsuitable</th>
<th>Edwards Sapien Transfemoral</th>
<th>Edwards Sapien Transapical</th>
<th>Edwards XT Transfemoral With Novaflex Delivery System</th>
<th>CoreValve</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Original PARTNER Trial Criteria 17–24-mm Annuli</td>
<td>Current IFU Criteria 18–25-mm Annuli</td>
<td>Current IFU Criteria 18–25-mm Annuli</td>
<td>Transfemoral</td>
</tr>
<tr>
<td>Annulus too small</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Annulus too large</td>
<td>26</td>
<td>12</td>
<td>26</td>
<td>12</td>
</tr>
<tr>
<td>Peripheries too small</td>
<td>60</td>
<td>60</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Aorta too large</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Total unsuitable</td>
<td>80</td>
<td>72</td>
<td>26</td>
<td>12</td>
</tr>
</tbody>
</table>

Values are presented as %.

IFU = instruction for use; PARTNER = Placement of Aortic Transcatheter valves trial.
systems will treat a wide range of patients (84% and 78%, respectively, in this series). This range is increased further for the respective devices by use of alternative approaches (89% and 88%, respectively).

It should be noted that with the combination of transfemoral devices available, the additional contribution of alternative access approaches (transapical for the Edwards Sapien system and transaxillary/direct aortic access for the Medtronic CoreValve system) is limited. We observed that 92% of cases were suitable for a multidevice transfemoral approach and only 5% more cases were afforded treatment by the addition of other approaches. This supports the rationale that TAVI should primarily be a catheterization laboratory-based transfemoral procedure, reserving other approaches for a minority. This is not presently the case for the Edwards Sapien system, which has a greater reliance on the transapical approach; the imminent reduction in device profile via the Novaflex system is likely to dramatically change practice (12). Conversely, proponents of the transapical approach point to an avoidance of extracardiac vascular complications (6).

**Evolution of the present mainstream TAVI devices.** Both currently available transcatheter aortic bioprostheses, Edwards Sapien and Medtronic CoreValve, are evolving their devices into smaller profiles to treat a wider range of annuli. The Edwards system miniaturization has been difficult in view of the balloon expandable design but is facilitated in part by the change in material of the stent frame from the stainless steel of the Edwards Sapien to the cobalt chromium of the Edwards XT. Also, the profile has been further reduced by an innovative Novaflex delivery system (Fig. 5) comprising a mechanism by which the stented valve is initially crimped on the catheter shaft and advanced to the level of the balloon in vivo for deployment (12). This has facilitated the reduction in profile from 22- to 18-F for the 23-mm prosthesis and from 24- to 19-F for the 26-mm prosthesis. These systems have already been used with success in Canada and Europe and are currently being evaluated in Europe in the PREVAIL (Prevention of VTE After Acute Ischemic Stroke With LMWH Enoxaparin) study. In addition, 20- and 29-mm prostheses are under development, but the time frame for these to come to fruition is unclear (Edwards Lifesciences, March 2010).

The Medtronic CoreValve system has a self-expanding prosthesis with a nitinol stent frame affording a low profile and early development of an 18-F system. Interestingly, the reduction in profile from the 21-F second-generation system to the 18-F present- (third-) generation system was facilitated by the replacement of bovine valve leaflets with those of porcine pericardial origin (18). There are 31- and 23-mm inflow devices in development that will expand the range of annuli to 27 to 29 mm and 18 to 20 mm, respectively. The company plans to eventually have the 23- and 26-mm inflow devices in a 16-F system, and the larger 2 in the 18-F system (Medtronic Inc., March 2010).
Qualitative versus quantitative suitability. The creation of multiple device sizes with similar access requirements will lead to the anatomic suitability of patients for both device types. However, qualitative differences will remain between the systems and will have an impact on clinical suitability. The tailoring of therapy will be increasingly relevant as more centers are trained in the implantation of multiple devices. For instance, the CoreValve device can be rapidly deployed without the need for rapid pacing and transesophageal echocardiography guidance, and it has a default leaflet configuration that is closed rather than open. This makes it the therapy of choice in the presence of hemodynamic instability.

A severely angulated ascending aorta or arch may favor an antegrade (transapical) approach, whereas cases with low coronary ostia may be more safely treated by the self-expanding design with its constrained central portion, provided the sinuses are not shallow. In contrast, a different aortic root morphology with shallow coronary sinuses may be better suited to the shorter-frame Edwards Sapien design. The use of multiple devices in TAVI centers will help to refine this complementary approach, with the relative strengths of each respective technology tailored to a particular patient.

Next-generation devices. Other valve companies, such as St. Jude Medical and Sorin, are rapidly developing their TAVI devices and it remains unclear as to which anatomic dimensions they will target (St. Jude Medical Inc., December 2009; Sorin Group, December 2009). A number of start-up companies including Sadra Medical (19), Direct Flow Medical (20), EndoLumix Technology (21), Heart Leaflet Technologies (22), JenaValve (23), Medtronic Ventor Technologies (24), and Symetis (25) have developed transfemoral devices as small as 14-F and can treat annuli well beyond the dimensions seen in our study (Table 2). The Palmaz-Bailey transcatheter valve promises an even smaller profile as low as 10-F, although the exact nature and time

![Figure 5. Newer Devices Studied](image)

(A) The Novaflex system. This new system facilitates reduction in profile for the Edwards XT device to 18- and 19-F for 23- and 26-mm prostheses, respectively. (A, Top) The stented valve is crimped ex vivo onto catheter shaft. (A, Middle) The delivery system facilitates advancement of stented valve onto balloon in vivo. (A, Bottom) The stented valve is deployed at the level of the aortic annulus. (B) The Medtronic Ventor system, a self-expanding transapical device.

### Table 2. Next-Generation Devices

<table>
<thead>
<tr>
<th>Device</th>
<th>Approach(es) Available</th>
<th>BE/SE/Other</th>
<th>Prosthesis Sizes (mm)</th>
<th>Range of Annuli Treatable (mm)</th>
<th>French Size of TF Delivery System</th>
</tr>
</thead>
<tbody>
<tr>
<td>EndoLumix*</td>
<td>TF</td>
<td>BE</td>
<td>20–25, 26–35</td>
<td>20–35</td>
<td>14/16</td>
</tr>
<tr>
<td>Direct Flow†</td>
<td>TF</td>
<td>Other</td>
<td>23, 25, 27</td>
<td>19–36</td>
<td>18</td>
</tr>
<tr>
<td>Heart Leaflet Technologies‡</td>
<td>TF</td>
<td>SE</td>
<td>21, 23, 25</td>
<td>19–25</td>
<td>17</td>
</tr>
<tr>
<td>JenaValve§</td>
<td>TA (TF to follow)</td>
<td>SE</td>
<td>21, 23, 25, 27</td>
<td>19–26.6</td>
<td>—</td>
</tr>
<tr>
<td>Ventor Engager (Medtronic Ventor)</td>
<td>TA</td>
<td>SE</td>
<td>23, 26, 29</td>
<td>19–28 mm (LVOT measurement)</td>
<td>—</td>
</tr>
<tr>
<td>Sadra Lotus¶</td>
<td>TF</td>
<td>SE</td>
<td>23, 27</td>
<td>19–26</td>
<td>18</td>
</tr>
</tbody>
</table>


BE = balloon expandable; LVOT = left ventricular outflow tract; SE = self-expanding; TA = transapical; TF = transfemoral.
frame for the clinical fruition of this device is unclear. Undoubtedly, these novel devices will further increase the range of patients anatomically suitable but their principal contribution will be through an increase in procedural simplicity and safety.

Study limitations. The study presented has only looked at 3 parameters of anatomic suitability that document the key anatomic inclusion and exclusion criteria. Other factors are relevant and include excessive femoral calcification and tortuosity, the severely hypertrophied septum and shallow or short aortic sinuses. These are special situations that deserve mention but, in terms of frequency, are not the principal anatomical limitations of TAVI today.

Our population, although bicentric, represented one of predominantly Caucasian ethnicity or large non-Caucasians, and populations of different ethnic distribution may have a greater reliance on transapical or alternative approaches to that of the femoral artery. Indeed, a study conducted by Schnyder et al. (26) in California suggested that there might be a lower incidence of female patients suitable for a present-day transfemoral TAVI approach, with femoral arteries greater than 6 mm in minimal dimension seen in only 50% of females in their series.

Conclusions

In the series presented, 97% of patients were anatomically suitable for a complementary approach to treatment by Edwards Lifesciences or Medtronic CoreValve devices. The 2-device strategy will offer TAVI to significantly more patients than a single-device service. The future expansion of device sizes will increase patient suitability for each system, and the variety of access approaches will ensure that the vast majority of patients can be treated. Having overcome anatomic constraints, the evolution of next-generation devices may best be directed toward procedural simplification and safety.

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REFERENCES


Key Words: anatomic selection ■ CoreValve ■ Edwards ■ transcatheter aortic valve implantation.