First implants with new Evolut PRO: advanced sealing for better performance

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Ospedale Mauriziano - Torino
### B) Choice of intervention in symptomatic aortic stenosis

Aortic valve interventions should only be performed in centres with both departments of cardiology and cardiac surgery on site and with structured collaboration between the two, including a Heart Team (heart valve centres).

The choice for intervention must be based on careful individual evaluation of technical suitability and weighing of risks and benefits of each modality (aspects to be considered are listed in Table 7). In addition, the local expertise and outcomes data for the given intervention must be taken into account.

SAVR is recommended in patients at low surgical risk (STS or EuroSCORE II < 4% or logistic EuroSCORE I < 10%\(^4\) and no other risk factors not included in these scores, such as frailty, porcelain aorta, sequelae of chest radiation).\(^93\)

TAVI is recommended in patients who are not suitable for SAVR as assessed by the Heart Team.\(^91, 94\)

In patients who are at increased surgical risk (STS or EuroSCORE II ≥ 4% or logistic EuroSCORE I ≥ 10%\(^4\) or other risk factors not included in these scores such as frailty, porcelain aorta, sequelae of chest radiation), the decision between SAVR and TAVI should be made by the Heart Team according to the individual patient characteristics (see Table 7), with TAVI being favoured in elderly patients suitable for transfemoral access.\(^91, 94–102\)
### ESC Guidelines

<table>
<thead>
<tr>
<th>Clinical characteristics</th>
<th>Favours TAVI</th>
<th>Favours SAVR</th>
</tr>
</thead>
<tbody>
<tr>
<td>STS/EuroSCORE II &lt;4% (logistic EuroSCORE I &lt;10%)</td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>STS/EuroSCORE II ≥4% (logistic EuroSCORE I ≥10%)</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Presence of severe comorbidity (not adequately reflected by scores)</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Age &lt;75 years</td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Age ≥75 years</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Previous cardiac surgery</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Frailty</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Restricted mobility and conditions that may affect the rehabilitation process after the procedure</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Susicion of endocarditis</td>
<td>+</td>
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</tbody>
</table>

### Anatomical and technical aspects

<table>
<thead>
<tr>
<th></th>
<th>+</th>
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</thead>
<tbody>
<tr>
<td>Favourable access for transfemoral TAVI</td>
<td>+</td>
</tr>
<tr>
<td>Unfavourable access (any) for TAVI</td>
<td></td>
</tr>
<tr>
<td>Sequelae of chest radiation</td>
<td>+</td>
</tr>
<tr>
<td>Porcelain aorta</td>
<td></td>
</tr>
<tr>
<td>Presence of intact coronary bypass grafts at risk when sternotomy is performed</td>
<td>+</td>
</tr>
<tr>
<td>Expected patient–prosthesis mismatch</td>
<td>+</td>
</tr>
<tr>
<td>Severe chest deformation or scoliosis</td>
<td>+</td>
</tr>
<tr>
<td>Short distance between coronary ostia and aortic valve annulus</td>
<td></td>
</tr>
<tr>
<td>Size of aortic valve annulus out of range for TAVI</td>
<td>+</td>
</tr>
<tr>
<td>Aortic root morphology unfavourable for TAVI</td>
<td>+</td>
</tr>
<tr>
<td>Valve morphology (bicuspid, degree of calcification, calcification pattern) unfavourable for TAVI</td>
<td>+</td>
</tr>
<tr>
<td>Presence of thrombi in aorta or LV</td>
<td>+</td>
</tr>
</tbody>
</table>
Paravalvular leak: Defining the problem
Impact on prognosis – Sapien Valve
High risk patients (PARTNER Trial)

- Mild, moderate, or severe vs. none or trace after TAVR was associated with increased late mortality (hazard ratio, 2.11; 95% CI, 1.43 to 3.10; P<0.001). Even mild aortic regurgitation was associated with an increased rate of late deaths.

- Moderate or severe paravalvular aortic regurgitation was more common after TAVR than after surgical replacement: 7.0% vs. 1.9% at 1 year, 6.9% vs. 0.9% at 2 years (P<0.001 for both comparisons).
Impact on prognosis - Sapien Valve
Intermediate risk patients (PARTNER 2 cohort A Trial)

In the TAVR group at 30 days, mild paravalvular aortic regurgitation was observed according to the standard classification scheme in 22.5% of patients, and moderate or severe paravalvular aortic regurgitation in 3.7%.

Patients in the TAVR group who had moderate or severe, but not mild, paravalvular aortic regurgitation at 30 days had higher mortality during 2 years of follow-up than did patients who had no or trace regurgitation (P<0.001).

Moderate or severe AR was associated with the lowest survival (45.2% at 5 years). There also appears to be an impact of mild AR on mortality demonstrated only after 2 years with a rate of 50.7% at 5 years.
**High-risk patients:**
Moderate to severe paravalvular regurgitation was higher in the TAVI group (6.1%), compared to surgical group (0.6%, p<0.001)

Reardon et al. JACC 2015;66:113-21 (Corevalve US Trial)

**Intermediate-risk patients:**
Moderate or severe paravalvular aortic regurgitation was more common after TAVR than after surgical replacement: 5.3% vs. 0.8% at 1 year, 5.7% vs. 1.2% at 2 years (P<0.001 for both comparisons).

Paravalvular leak: Defining the problem

- Sapien XT Partner IIB N=236
- Sapien Partner IIB N=225
- CoreValve Extreme Risk N=418
- CoreValve High Risk Portico CE Study N=75
- Sapien 3 Partner II N=1504
- Evolut R CE Study N=60
- Lotus Reprise II + Ext N=177
- Sapien XT Partner IIB IR N=1011
- SURTAVI (CoreValve)

% Patients with moderate/severe PVL at 30 days

References:
Risk factors for PVL after TAVI

Anatomical factors
- Bicuspid aortic valve
- Aortic annulus dimensions (perimeter, diameter)
- Annulus shape (eccentricity)
- LVOT-AO angle
- Extent and distribution of calcifications
- Calcification of commissures

Procedure and operator-dep. factors
- Undersizing of the device
- Malpositioning of the valve
- Depth of implantation
- Learning curve

**Advanced Sealing**

**Conformable Frame**
Self-expanding nitinol frame conforms to annulus regardless of shape

**Consistent Radial Force**
Frame oversizing and cell geometry provide consistent radial force across treatable range

**External Wrap**
External wrap increases surface contact with native anatomy

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CoreValve | Evolut R | Evolut PRO
Animal Studies suggest favorable Response and Interaction with Native Tissue

- Low inflammatory response\(^1\)
- **Stable and mature tissue growth** observed at 90 days post implant\(^1\)
  - Thin and even layer of endothelial cells on inner lumen of device

Evolut PRO explanted from Porcine Model at 60 Days, Cross Section between Nodes 1 and 2, example picture from MDT research study on file illustrating tissue interaction.\(^2\)

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1. Medtronic data on file. 90 day porcine GLP Evolut R study, results may not be indicative of clinical performance
2. Medtronic, data on file. 60 day porcine research study model, results may not be indicative of clinical performance.
**EVOLUT PLATFORM**

<table>
<thead>
<tr>
<th>Diameter (mm)</th>
<th>18</th>
<th>19</th>
<th>20</th>
<th>21</th>
<th>22</th>
<th>23</th>
<th>24</th>
<th>25</th>
<th>26</th>
<th>27</th>
<th>28</th>
<th>29</th>
<th>30</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perimeter (mm)†</td>
<td>56.5</td>
<td>62.8</td>
<td>72.3</td>
<td>81.7</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>94.2</td>
</tr>
</tbody>
</table>

* Based on CT measurement
† Annulus Perimeter = Annulus Diameter x \( \pi \)

**Vessel Access (mm)**

| 5.5 |

**French Size**

| 16 Fr eq |
## EVOLUT PRO SYSTEM CLINICAL TRIAL

### PATIENT CHARACTERISTICS

<table>
<thead>
<tr>
<th>Characteristic, mean ± SD or %</th>
<th>N=60</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>83.3 ± 7.2</td>
</tr>
<tr>
<td>Female</td>
<td>65.0</td>
</tr>
<tr>
<td>BSA, m²</td>
<td>1.8 ± 0.2</td>
</tr>
<tr>
<td>STS – PROM, %</td>
<td>6.4 ± 3.9</td>
</tr>
<tr>
<td>NYHA Class III or IV</td>
<td>70.0</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>43.3</td>
</tr>
<tr>
<td>Atrial fibrillation / atrial flutter</td>
<td>18.6</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>43.3</td>
</tr>
<tr>
<td>Severe aortic calcification</td>
<td>20.5</td>
</tr>
<tr>
<td>LV ejection fraction, %</td>
<td>58.9 ± 12.4</td>
</tr>
<tr>
<td>Pre-existing pacemaker</td>
<td>15.0</td>
</tr>
</tbody>
</table>

Forrest, et al., ACC, 2017
# EVOLUT PRO SYSTEM CLINICAL TRIAL

## PROCEDURAL OUTCOMES

<table>
<thead>
<tr>
<th>Characteristic, % or mean ± SD</th>
<th>N = 60</th>
</tr>
</thead>
<tbody>
<tr>
<td>General anesthesia</td>
<td>58.3</td>
</tr>
<tr>
<td>Iliofemoral access approach</td>
<td>98.3</td>
</tr>
<tr>
<td>Valve Size Implanted</td>
<td></td>
</tr>
<tr>
<td>26 mm</td>
<td>40.0</td>
</tr>
<tr>
<td>29 mm</td>
<td>60.0</td>
</tr>
<tr>
<td>Pre-TAVR balloon dilation</td>
<td>51.7</td>
</tr>
<tr>
<td>Post-implant balloon dilation</td>
<td>26.7</td>
</tr>
<tr>
<td>Percentage of patients repositioned</td>
<td>35.0</td>
</tr>
<tr>
<td>Average implant depth, mm</td>
<td>4.3 ± 1.6</td>
</tr>
</tbody>
</table>

Forrest, et al., ACC, 2017
EVOLUT PRO SYSTEM CLINICAL TRIAL

Forrest, et al., ACC, 2017
EVOLUT PRO PARAVALVULAR PERFORMANCE
30 DAYS

NOTE: PVL performance data represent different device performance in different trials; comparison of results is for illustration purposes only and may not be indicative of clinical performance.


- CoreValve US IDE (HR)\(^1\) N = 391
  - None/Trace: 1.7%
  - Mild: 7.3%
  - Moderate: 35.7%
  - Severe: 55.3%

- Evolut R US Evolut R Trial\(^2\) N = 233
  - None/Trace: 5.7%
  - Mild: 32.6%
  - Moderate: 61.6%
  - Severe: 7.3%

- Evolut PRO US Evolut PRO Trial\(^3\) N = 58
  - None/Trace: 2.7%
  - Mild: 27.6%
  - Moderate: 72.4%
Sex: Male  Age: 85

Clinical symptoms

• Angina and Cardiac decompensation with dyspnea, weakness, dizziness

Medical History

• COPD
• Hypertension
• Previous smoke
• CAD familiar history
• Peripheral artery disease
• Chronic kidney disease
• Paroxymal atrial fibrillation (Rivaroxaban)
• Active lifestyle and normal mental status
• CAD: 06/2017 --> PCI + DES on LCx and RCA

Echo

• Severe Aortic Stenosis (Pmax 77 mmHg, Pmed 47 mmHg, AVA 0.51 cm²) and moderate aortic regurgitation
• Trivial mitral and tricuspid regurgitation
• Mild pulmonary hypertension (PAPs 36 mmHg)

Lab

• Creatinine 1.94 mg/dl (eGFR) 30 ml/min
• Hb 13.1
• PLTS 269
• ALB 34
Heart Team

Risk scores:

- STS Score: Risk of Mortality 4.055%, Risk of Morbidity or Mortality 24.94%
- Logistic Euroscore: 13.69%

Coronary angio
CT evaluation

Aortic annulus:
- Perimeter 74 mm
- Area 0.41 cm²

Sinotubular junction 33 mm

Diameter
Aortography

Peak-to-peak gradient: 60 mmHg
Evolut PRO 29 mm implantation
Evolut PRO 29 mm implantation
Pressure gradient after implantation

Peak-to-peak gradient: 17 mmHg

Mean gradient: 19 mmHg
Evolut PRO 29 mm postdilation
Pressure-Gradient after postdilation

Peak-to-peak gradient: 5 mmHg

Mean gradient: 7 mmHg
First experience at Mauriziano Hospital: Pt #2

Sex: Female  
Age: 82

Clinical symptoms
- Cardiac decompensation and dyspnea (NYHA III)

Medical History
- Hypertension
- Previous smoke
- CAD familiar history
- Peripheral artery disease
- Ascending aorta aneurysm
- Chronic kidney disease (Grade III)
- Permanent atrial fibrillation (Warfarin)
- Active lifestyle and normal mental status

Echo
- Severe Aortic Stenosis (Pmax 80 mmHg, Pmed 50 mmHg, AVA 0.40 cm$^2$) and mild aortic regurgitation
- Moderate mitral stenosis and regurgitation, moderate tricuspid regurgitation
- Severe pulmonary hypertension (PAPs 55 mmHg)

Lab
- Creatinine 0.9 mg/dl (eGFR) 57 ml/min
- Hb 11
- PLTS 284
- ALB 34
Heart Team

Risk scores:

- STS Score: Risk of Mortality 4.55%, Risk of Morbidity or Mortality 29.4%
- Logistic Euroscore: 16.43%

Coronary angio
CT evaluation

Aortic annulus:
- Perimeter 74 mm
- Area 0.41 cm²

Sinotubular junction 38 mm
Diameters: 24 mm × 21 mm
Evolut PRO 29 mm implantation
Evolut PRO 29 mm implantation
**Sex:** Female  
**Age:** 89

**Clinical symptoms**
- Cardiac decompensation with acute renal failure, dyspnea (NYHA III)

**Medical History**
- Hypertension
- Peripheral artery disease
- Chronic kidney disease (Grade II)
- Active lifestyle and normal mental status

**Echo**
- Severe Aortic Stenosis (Pmax 68 mmHg, Pmed 40 mmHg, AVA 0.60 cm²) and mild aortic regurgitation
- Mild mitral and tricuspid regurgitation
- No pulmonary hypertension (PAPs 25 mmHg)

**Lab**
- Creatinine 0.82 mg/dl (eGFR) 63 ml/min
- Hb 11.1
- PLTS 262
- ALB 36

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First experience at Mauriziano Hospital: Pt #3
Heart Team

Risk scores:

• STS Score: Risk of Mortality 4.85%, Risk of Morbidity or Mortality 38.7%

• Logistic Euroscore: 31.51%

Coronary angio
**Angio and CT evaluation**

**Aortic annulus:**
- Perimeter 77 mm
- Area 0.44 cm$^2$

**Sinotubular junction**
- 36 mm

Diameters: 25 mm X 20 mm
Evolut PRO 29 mm implantation
Evolut PRO 29 mm implantation
Estimated Global TAVI Procedure Growth

SOURCE: Credit Suisse TAVI Comment –January 8, 2015. ASP assumption for 2024 and 2025 based on analyst model. Revenue split assumption in 2025 is 45% U.S., 35% EU, 10% Japan, 10% ROW