TAVR for Complex Aortic Valvular Conditions

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Penn Aortic Valve Repair Symposium
September 2016
Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

<table>
<thead>
<tr>
<th>Affiliation/Financial Relationship</th>
<th>Company</th>
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<tbody>
<tr>
<td>Grant/Research Support</td>
<td>Edwards Lifesciences, Medtronic, Livanova, W.L.Gore, Bolton Medical</td>
</tr>
<tr>
<td>Consulting Fees/Honoraria</td>
<td>Microinterventional Device</td>
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A BREAKDOWN OF OUR 1,000 TAVR CASES

Nov. 2007 – Jan. 2015

PARTNER Trial (N=475)

PARTNER 1 (n=185)
- 115 TF
- 70 TA

PARTNER 2

P2A (n=39)
- 25 TF
- 1 TAO
- 13 TA

P2B (n=140)
- 112 TF
- 4 TAO
- 24 TA

Commercial TAVR Cases (N=518)
- 368 TF
- 150 Alternative Access
- 337 Sapien (65.1%)
- 95 Sapien XT (18.3%)
- 86 Corevalve (16.6%)

Sapien 3

SURTAVI (N=7)
- 6 TF
- 1 Alternative Access

High Risk (n=45)
- 32 TF
- 3 TAO
- 10 TA

Intermediate Risk (n=66)
- 60 TF
- 1 TAO
- 5 TA
A Look Back Over the Beginning of TAVR at UPHS

TAVR November 2007 to November 2015

CoreValve
SurTAVI

LOTUS
S3
PORTICO

Sapien Commercial Approved 2011

Sapien XT
Partner II

Partner I
TA 9/2008

11/2009 PPMC

Nov 2007

2 19 55 110 224 449 666 971 1271
Heart Valve Team

Repair

Sutureless

TAVR

MIS

Hybrid
Patient Selection
TAVR vs AVR

Operable AS patients

Low-Intermediate Risk

90%

High Risk

10%

Too Sick

Inoperable

A
High Risk

B
Extreme Risk

C

%?
PARTNER II trial

Transcatheter or Surgical Aortic-Valve Replacement in Intermediate-Risk Patients


Transcatheter aortic valve replacement versus surgical valve replacement in intermediate-risk patients: a propensity score analysis

The PARTNER 3 Trial
Study Design

1:1 Randomization (n=1228)
TF - TAVR (SAPIEN 3)
SAVR (Surgical Bioprosthetic Valve)
Follow-up: 30 day, 6 mos, 1 year and annually through 10 years
CT Imaging Sub-Study (n=200)
Activity/QoL Sub-Study (n=100)

Low Risk ASSESSMENT by Heart Team (STS < 4%)

Symptomatic/Asymptomatic Severe Calcific Aortic Stenosis

PARTNER 3 Registries

Bicuspid (n=100)
ViV (n=100)

Alternative Access (n=100) (TA/Tae/Subclavian)

PRIMARY ENDPOINT:
Composite of all-cause mortality, all stroke, or re-hospitalization at 1 year post procedure
MEDTRONIC TAVR IN LOW RISK PATIENTS
TRIAL DESIGN & LEAFLET SUB-STUDY

- **Patient Population: Low Risk Cohort**
  - Determined by Heart Team to be low surgical risk

- **Primary Endpoint:**
  - Safety: Death, all stroke, life-threatening bleeding, major vascular complications, or AKI at 30 days
  - Efficacy: Death or major stroke at 2 years

- **Sample Size:** ~1200 Subjects

- **Follow-up Evaluations:**
  - 30-days, 6-month, 18-month, and 1 Through 5 years

- **Number of Sites:** Up to 80 sites
PARTNER 2 A
Primary Endpoint (ITT)
All-Cause Mortality or Disabling Stroke

HR [95% CI] = 0.89 [0.73, 1.09]
p (log rank) = 0.253
Evolution of the “Minimalist” Approach

- Femoral cutdown to percutaneous
- Postoperative recovery from ICU to fast track
- General anesthesia (GA) to conscious sedation (CS) / monitored anesthesia care (MAC)

Heart Team Is Intact
Percutaneous Access
TF Completed with MAC or GA

- First Quintile of Analysis (April to July 2014)
TF Completed with MAC or GA

- Last Quintile of Analysis (Aug. to Nov. 2015)
Expanding the Indications
Practice Gaps

- Low risk
- Significant MR / TR
- Renal failure / Dialysis
- Bicuspid aortic valve
- Aortic Insufficiency
Bicuspid Aortic Valve

Stenosis

Regurgitation
Bicuspid Aortic Valve
Bicuspid Aortic Valve
Transcatheter Aortic Valve Replacement in Bicuspid Aortic Valve Disease

Darren Mylotte, MB, MD,*† Thierry Lefevre, MD;† Lars Søndergaard, MD;§ Yusuke Watanabe, MD;† Thomas Modine, MD,|| Danny Dvir, MD;¶ Johan Bosmans, MD;# Didier Tchetché, MD;** Ran Kornowski, MD;†† Jan-Malte Sinning, MD;‡‡ Pascal Thériault-Lauzier, PhD;† Crochan J. O’Sullivan, MB, MD;§§ Marco Barbanti, MD,|||| Nicolas Debruy, MD; Jean Buithieu, MD; Pablo Codner, MD,†† Magdalena Dorfmeister, MD;¶¶ Giuseppe Martucci, MD;† Georg Nickenig, MD;‡‡ Peter Wenaweser, MD;§§ Corrado Tamburino, MD;||| Eberhard Grube, MD;‡‡ John G. Webb, MD;¶ Stephan Windecker, MD;§§ Rüdiger Lange, MD, PhD;¶¶ Nico Piazza, MD, PhD;¶¶

JACC 2014

Postimplantation echocardiography

Aortic regurgitation, grade (1–4)* 1.1 ± 0.9

≥ Grade 2 38 (28.4)

≥ Grade 3 8 (6.0)

Aortic valve gradient, mm Hg* 11.4 ± 9.9

Aortic valve area, cm²* 1.7 ± 0.5

Contrast media, ml 174 ± 88

Fluoroscopy duration, min 20 (14–28)
## Bicuspid AV and TAVR

### Table 4
Long-term results

<table>
<thead>
<tr>
<th></th>
<th>BAV (n = 23)</th>
<th>No-BAV (n = 70)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follow-up (months)</td>
<td>11.4 ± 1.3</td>
<td>11.6 ± 1.5</td>
<td>1.00</td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>5 (18%)</td>
<td>14 (17%)</td>
<td>1.00</td>
</tr>
<tr>
<td>All-cause mortality in patients with PVLR &lt;2*</td>
<td>2 (11%)</td>
<td>10 (15%)</td>
<td>0.72</td>
</tr>
<tr>
<td>All-cause mortality in patients with PVLR ≥2†</td>
<td>3 (33%)</td>
<td>4 (21%)</td>
<td>0.36</td>
</tr>
<tr>
<td>New York Heart Association class at follow-up</td>
<td>1.6 ± 0.6</td>
<td>1.8 ± 0.6</td>
<td>0.23</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>53.5 ± 18.1</td>
<td>51.1 ± 12.7</td>
<td>0.53</td>
</tr>
<tr>
<td>Aortic prosthetic valve area (cm²)</td>
<td>1.6 ± 0.4</td>
<td>1.7 ± 0.3</td>
<td>0.73</td>
</tr>
<tr>
<td>Mean gradient (mm Hg)</td>
<td>10.3 ± 5.4</td>
<td>9.8 ± 2.8</td>
<td>0.64</td>
</tr>
<tr>
<td>Aortic regurgitation ≥2</td>
<td>6 (22%)</td>
<td>17 (22%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Mitral regurgitation ≥2</td>
<td>5 (19%)</td>
<td>25 (32%)</td>
<td>0.32</td>
</tr>
</tbody>
</table>

*Significantly different from baseline at follow-up.
†Significantly better in BAV than in No-BAV group.

Kochman et al, JACC, 2014
Durability / Long Term Outcome

No Data?
First look at long-term durability of transcatheter heart valves: Assessment of valve function up to 10-years after implantation

Danny Dvir, St. Paul’s Hospital, Vancouver, Canada.

On behalf of coauthors: Helene Etchaninoff, Jian Ye, Arohumam Kan, Eric Durand, Anna Bizios, Anson Cheung, Mina Aziz, Matheus Simonato, Christophe Tron, Yaron Arbel, Robert Moss, Jonathon Leipsic, Hadas Ofek, Gidon Perlman, Marco Barbanti, Michael A. Seidman, Philippe Blanke, Robert Yao, Robert Boone, Sandra Lauck, Sam Lichtenstein, David Wood, Alain Cribier, John Webb
Freedom from THV degeneration

THV degeneration was defined as at least moderate regurgitation AND/OR mean gradient ≥ 20mmHg, which did not appear within 30 days of the procedure and is not related to endocarditis.

KM estimate of THV degeneration included censoring of patients at their date of last known THV functioning well without evidence for degeneration per study definition.

THV degeneration (at least moderate stenosis AND/OR regurgitation) was ~50% within 8 years.
The PARTNER 3 Trial
Study Design

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(STS < 4%)

1:1 Randomization (n=1228)

TF - TAVR
(SAPIEN 3)

SAVR
(Surgical Bioprosthetic Valve)

Follow-up: 30 day, 6 mos, 1 year and annually through 10 years

PRIMARY ENDPOINT:
Composite of all-cause mortality, all stroke, or re-hospitalization at 1 year post procedure
Aortic Insufficiency
History of Homograft
Initial German Experience With Transapical Implantation of a Second-Generation Transcatheter Heart Valve for the Treatment of Aortic Regurgitation

Moritz Seiffert, MD,* Ralf Bader, MD,† Utz Kappert, MD,‡ Ardawan Rastan, MD,§ Stephan Krapf, MD,|| Sabine Bleiziffer, MD,¶ Steffen Hofmann, MD,# Martin Amold, MD,** Klaus Kallenbach, MD,†† Lenard Conradi, MD,* Friederike Schlingloff, MD,† Manuel Wilbring, MD,‡ Ulrich Schäfer, MD,† Patrick Diemert, MD,* Hendrik Treede, MD*
### High Risk AR / AI Patients

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>NYHA functional class &gt; III</td>
<td>12 (38.7)</td>
</tr>
<tr>
<td>Ascending aortic diameter, mm†</td>
<td>36.6 ± 7.0 (20/31)</td>
</tr>
<tr>
<td>Aortic regurgitation mode</td>
<td></td>
</tr>
<tr>
<td>Annular dilation</td>
<td>6 (19.3)</td>
</tr>
<tr>
<td>Degenerative</td>
<td>15 (48.4)</td>
</tr>
<tr>
<td>Post-endocarditis</td>
<td>4 (12.9)</td>
</tr>
<tr>
<td>Rheumatic</td>
<td>1 (3.2)</td>
</tr>
<tr>
<td>Post-radiation therapy</td>
<td>1 (3.2)</td>
</tr>
<tr>
<td>Unknown</td>
<td>4 (12.9)</td>
</tr>
<tr>
<td>Aortic regurgitation grade</td>
<td></td>
</tr>
<tr>
<td>None or mild</td>
<td>0</td>
</tr>
<tr>
<td>Moderate</td>
<td>1 (3.2)</td>
</tr>
<tr>
<td>Severe</td>
<td>30 (96.8)</td>
</tr>
</tbody>
</table>

**Severe AI 96%**

Minimal calcification / stenosis

**Figure 1:** Aortic Annulus, Root, and Valve Morphology Assessed by Contrast-Enhanced MSCT and TEE
Cardiac 30D Mortality: 1 (3.2%)
Stroke: 0 (0%)
Device Success: 30 (96%)
Case Report

Critical Aortic Stenosis and Acute Ascending Aortic Penetrating Ulcer Managed Utilizing Transapical TAVR and TEVAR

Keith B. Allen,1* MD, J. Russell Davis,1 MD, and David J. Cohen,2 MD

Thoracic endovascular aortic repair (TEVAR) of acute ascending aortic pathology is feasible; however, the unique features of this aortic segment in addition to access challenges restrict its use to a select, high-risk subset of patients. With the advent of TAVR, large device delivery using transapical access has become a well-defined technique. We report a patient with critical aortic stenosis and an acute ascending aortic penetrating ulcer with tamponade managed successfully utilizing transapical TAVR and TEVAR. To our knowledge, this is the first reported case of a hybrid single-stage TAVR and ascending aortic TEVAR using transapical access.

Key words: endovascular, ascending aorta; transcatheter valve

Catheterization and Cardiovascular Interventions 00:00–00 (2015)
-1 to 1 Landing Zone Concept

Endobentall

Endo Arch

Synergy

TAVR/TEVAR
Transcatheter Mitral Therapies
Vital Components to a Successful Transcatheter Valve Program

The Heart Team

Penn Physicians:
- Cardiovascular Surgeons
- Interventional Cardiologists
- Echocardiologists
- CT anesthesiologists

Outside Referring Physicians

Hybrid OR Staff
- ICU Nurses
- Research Coordinators

Sponsoring Company
- Patient Families

Team Work