Discussion: FRANCE-TAVI registry

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Disclosures

None
SAVR

High-risk
Intermediate-risk
Low-risk

TAVR

Inoperable/Extreme-risk

Which valve? Class effect?

Mechanical valve
Asymptomatic
Bicuspid AS

Otto CM, Kumbhani DJ. JACC 2017
**SOLVE-TAVI**

STS 7.8%
Sapien S3 (n=219) vs. Evolut R (n=219)

- 30-DAY MOD/SEVERE PVL: Sapien S3 1.9 vs. Evolut R 2.3, p=0.77
- 30-DAY MORTALITY: Sapien S3 1.4 vs. Evolut R 2.8, p>0.99

Thiele H. TCT 2018

**CHOICE**

STS ≥ 10%/inoperable
Sapien XT (n=121) vs. CoreValve (n=120)

- 30-DAY MOD/SEVERE PVL: Sapien XT 4.1 vs. CoreValve 5.1, p=0.77
- 30-DAY MORTALITY: Sapien XT 4.1 vs. CoreValve 5.1
- 1-YEAR MORTALITY: CoreValve 12.8

Abdel-Wahab M. JAMA 2014; Abdel-Wahab M. JACC 2015

**CENTER registry**

STS 6.5%
BE (n=4,096) vs. SE (n=4,096)*

- 30-DAY MOD/SEVERE PVL: BE 5.3 vs. SE 3.1
- 30-DAY MORTALITY: BE 6.2 vs. SE 3.4
- 30-DAY MORTALITY (S3/EV): BE 3.1 vs. SE 3.4, p=0.73

*Propensity-matched

Vlastra W. EHJ 2019
FRANCE-TAVI registry

- 2013-2015
- 48/50 sites
- EuroSCORE: 14.5%
- High risk: 37%
- TF access: 81%
- Conscious sedation: 47%
- No ViV

- BE (n=3910) vs. SE (n=3910)
- Sapien S3 (n=2440) vs. Evolut (2,435)

- IN-HOSP MOD/SEVERE PVL
  - 8.3
  - 4.2

- IN-HOSP MORTALITY
  - 15.5
  - 5.6

- 2-YEAR MORTALITY
  - 29.8

p<0.001
p=0.002
p=0.01
p=0.001

IN-HOSP MOD/SEVERE PVL
IN-HOSP MORTALITY
2-YEAR MORTALITY

CV mortality
Things to consider

• Hazardous to make causal inferences from observational data

• Biological plausibility
  • Valve design: Less radial strength with SE vs. BE
  • Association of PVL with mortality
Severity of PVL at 30 Days and All-cause Mortality at 2 Years

Number at risk:
- Moderate/Severe: 36
- Mild: 210
- None/Trace: 701

All-Cause Mortality (%)

- Months from Procedure
  - 0: 14.1%
  - 10: 13.5%
  - 20: 34.0%
  - 30: 34.0%

Overall Log-Rank p = 0.001
Mod/Sev (reference = None/Trace)
p (Log-Rank) < 0.001

Mild (reference = None/Trace)
p (Log-Rank) = 0.82

Kodali S. NEJM 2012
Things to consider

• Hazardous to make causal inferences from observational data

• Biological plausibility
  • Valve design: Less radial strength with SE vs. BE
  • Association of PVL with mortality
  • Early hazard: patient or device? Are sicker patients receiving SE valves?
  • Other complications: ↑ pacemaker rate with SE vs. BE – can impact mortality
  • Valve hemodynamics, EOA ↑, patient-prosthesis mismatch ↓ with SE vs. BE

• Not completely contemporary (2015; valve generations?), no echo core lab

• Other more recent data

Hahn R. JACC CV Img. 2019
Herrmann H. JACC 2018
Kumbhani DJ. JACC 2016
Echocardiographic Valve Performance

**Paravalvular Aortic Regurgitation**

- P < 0.0001
- ACURATE neo (n = 361)
  - ≥ moderate: 9.4%
  - mild: 50.1%
  - none: 40.4%

- SAPIEN 3 (n = 363)
  - ≥ moderate: 2.8%
  - mild: 31.1%
  - none: 66.1%

**Mean Gradient ≥20 mmHg AND EOA ≤ 0.9-1.1 cm² and/or DVI < 0.35**

- P = 0.06
- ACURATE neo (n = 361)
  - yes: 0.6%
  - no: 99.4%

- SAPIEN 3 (n = 363)
  - yes: 2.2%
  - no: 97.8%

**Mortality**

2.5% vs. 0.8%, p=0.09
### FlexNav DS Cohort: Clinical Outcomes at 30 Days

**Primary endpoint: 7% major vascular complications**

<table>
<thead>
<tr>
<th>VARC 2 Endpoint</th>
<th>RCT Portico valve (N=381)</th>
<th>RCT Commercial valve (N=369)</th>
<th>FlexNav DS Cohort (N=100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-Cause Mortality</td>
<td>3.5%</td>
<td>1.9%</td>
<td>0.0%</td>
</tr>
<tr>
<td>Cardiovascular Mortality</td>
<td>3.2%</td>
<td>1.7%</td>
<td>0.0%</td>
</tr>
<tr>
<td>Disabling Stroke</td>
<td>1.6%</td>
<td>1.1%</td>
<td>0.0%</td>
</tr>
<tr>
<td>Life-Threatening Bleeding Requiring Transfusion</td>
<td>4.5%</td>
<td>3.6%</td>
<td>4.0%</td>
</tr>
<tr>
<td>Acute Kidney Injury Requiring Dialysis</td>
<td>1.1%</td>
<td>0.8%</td>
<td>0.0%</td>
</tr>
<tr>
<td>Major Vascular Complications</td>
<td>9.6%</td>
<td>6.3%</td>
<td>7.0%</td>
</tr>
<tr>
<td>New PPI</td>
<td>27.7%</td>
<td>11.6%</td>
<td>14.6%</td>
</tr>
<tr>
<td>Moderate or Greater PVL</td>
<td>6.3%</td>
<td>2.1%</td>
<td>6.5%</td>
</tr>
</tbody>
</table>
Design considerations

• Statistical methods appropriate
• IPTW similar results
• Falsification endpoint analysis similar
• Despite this, possibility of residual confounding exists
Final thoughts

• Intriguing analysis

• Inherent differences between TAVR valves
  • May be incorrect to assume a class effect
  • Important to match patient to valve

• The field urgently needs head-to-head comparison trials
  • Device success (PVL), complications (pacemaker)
  • Hemodynamic performance (EOA, gradients)
  • Hard endpoints: long-term important as we expand the eligible patient pool
  • Cost
High risk or inoperable: 15%
Intermediate risk: 35%
Low risk: 50%

STS < 3%
FDA approval: August 16, 2019

STS 3-8%
FDA approval: August 18, 2016

STS => 8%
FDA approval: Nov 2, 2011/October 19, 2012