Updates on transcatheter aortic and mitral valve replacement: indications, patient selection, long term result

Dr Jack Tan
Immediate Past President Singapore Cardiac Society
President Asian Pacific Society of Cardiology

10th Central Vietnam Open Congress of Cardiology
Disclosure Statement of Financial Interest

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

Affiliation/Financial Relationship
- Grant/Research Support
- Consulting Fees/Honoraria

Company
- Abbott Diagnostics, Beckmann, Bayer, Roche, AZ
- Alvimedica, Orbus Neich, Medtronic, Abbott Vascular, Elixir, Boston Scientific, Sanofi, Bayer, Boehringer Ingelheim, AstraZenica, Amgen
Outline: Focus on TAVR and Mitra-Clip

- Overview
- Indications
- Anatomy
- Procedure
- Safety
- Evidence so far
- Functional MR
MitraClip®
Transcatheter Mitral Valve Repair

100 PATIENTS TREATED!

National Heart Centre Singapore
SingHealth

Abbott
#1: Overview

- Percutaneous edge-to-edge repair
- Double-orifice technique – Alfieri stitch
- Clinical use since 2008
MitraClip System
MitraClip Procedure
#2: Indications

- Moderate-to-severe or severe (3 to 4+) MR
- Symptomatic
- High or prohibitive surgical risk
- Types of MR
  - USA: DMR
  - Rest of the world: DMR and FMR
- Heart Team Discussion
What do the guidelines say?

2017 ESC/EACTS Guidelines for the management of valvular heart disease

The Task Force for the Management of Valvular Heart Disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)
Percutaneous edge-to-edge procedure may be considered in patients with symptomatic severe primary mitral regurgitation who fulfill the echocardiographic criteria of eligibility and are judged inoperable or at high surgical risk by the Heart Team, avoiding futility.

In patients with severe secondary mitral regurgitation and LVEF <30% who remain symptomatic despite optimal medical management (including CRT if indicated) and who have no option for revascularization, the Heart Team may consider a percutaneous edge-to-edge procedure or valve surgery after careful evaluation for a ventricular assist device or heart transplant according to individual patient characteristics.
Transcatheter mitral valve repair may be considered for severely symptomatic patients (NYHA class III to IV) with chronic severe primary MR (stage D) who have favorable anatomy for the repair procedure and a reasonable life expectancy but who have a prohibitive surgical risk because of severe comorbidities and remain severely symptomatic despite optimal GDMT for heart failure (HF) (124).
<table>
<thead>
<tr>
<th>Too soon</th>
<th>?</th>
<th>Ideal</th>
<th>?</th>
<th>Too late</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>II</td>
<td>III</td>
<td>IV</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**NYHA class**

- Too soon
- Ideal
- Too late

**LV impairment**

- RV impairment
- TR
- PAH

**Intermittent IV**

**Chronic IV**

**Shock**

Judging the appropriate timing
3 Patients with EROA of 30 mm²

LVAD, transplant, hospice

LVEF 22%
LVEDV 310 mL
GLS -6.8%

LVEF 36%
LVEDV 197 mL
GLS -8.4%

LVEF 60%
LVEDV 140 mL
GLS -20.3%

LVEF, LV size, LV geometry
Severely abnormal

LVEF, LV size, LV geometry
Mild-to-moderately abnormal

LVEF, LV size, LV geometry
Normal

Spectrum of LV dysfunction

MR correction likely to be beneficial
#3: Anatomy

- **Easy / Classical:** A2/P2, central MR
- **Difficult:** Eccentric jets, A3/P3, A1/P1, broad MR, extensive flail, ASD/PFO
- **Very difficult:** Commissural, cleft (?)
- **Contraindicated:** Endocarditis, significant MS
Figure 2: Ideal morphologies for a MitraClip implantation. The pathology should be located in the middle segments (A and D) with no calcification in the grasping area as shown in an intercommissural view in (D). (B) Illustrates some remaining degree of coaptation (red arrows, ideally at least 2 mm), the yellow line represents the coaptation depth (ideally < 11 mm). The yellow arrow in (C) follows a posterior leaflet with enough tissue for grasping (ideally ≥ 10 mm) and the red arrow illustrates the measurement of a flail gap (ideally < 10 mm). In (E), the flail width is marked with a red arrow (ideally < 15 mm) (P2 prolapse in a non-surgical view).
#4: Procedure

- General anesthesia
- Transesophageal echo: High technical skill
- Proceduralist: 2 operators (usually)
- Communication is CRITICAL
- Anesthetist
- Nursing expertise
Procedure Imaging

MitraClip® Procedure is Driven by Echocardiography

**Echocardiography**
(Primary Imaging)

**Fluoroscopy**
(Secondary Imaging)
#5: Safety

- Generally very safe
- Bleeding
- Single leaflet or complete detachment
- Leaflet or chordal damage
- ASD
- CVA
#6: Evidence so far

- EVEREST II: Not as good as surgery for MR reduction
- Efficacious for symptom relief
- Real-world experience excellent
- Steep learning curve
#7: Evidence so far

- Landmark RCT – Feasibility and Safety of MitraClip
- Surgery (Gold Standard) remains superior to MitraClip in MR reduction
- Mortality similar
- MR reduction by MitraClip showed clinical benefits (NYHA, QoL, and Echo volumes)
Randomized Comparison of Percutaneous Repair and Surgery for Mitral Regurgitation

5-Year Results of EVEREST II

Ted Feldman, MD,* Saibal Kar, MD,† Sammy Elmariah, MD, MPH, §§ Steven C. Smart, MD,* Alfredo Trento, MD,||
Robert J. Siegel, MD,† Patricia Apruzzese, MS,§ Peter Fail, MD,¶ Michael J. Rinaldi, MD,#
Richard W. Smalling, MD, Ph.D,,** James B. Herrmiller, MD,†† David Heimansohn, MD,†† William A. Gray, MD,§§
Paul A. Grayburn, MD,||| Michael J. Mack, MD,¶¶ D. Scott Lim, MD,## Gorav Ailawadi, MD,***
Howard C. Herrmann, MD,††† Michael A. Acker, MD,++++ Frank E. Silvestry, MD,††† Elyse Foster, MD,§§§
Andrew Wang, MD,|||| Donald D. Glower, MD,¶¶¶ Laura Mauri, MD,§§§§ for the EVEREST II Investigators
• Once again, similar to 1 year results
  • Mortality similar with both groups
  • Symptoms and QOL improved with both techniques
• Durability of MR reduction with MitraClip
  • Despite early imbalance in rates of MR 3-4+ and subsequent surgery for MV dysfunction, few patients (n=10 of 43) experienced worsening MR or surgery after 6-month follow-up
  • Clinical failures occur in 1st 6 months, most of which from inadequate MR reduction during index procedure or early SLDA (likely an issue of learning curve as acute procedural success and SLDA rates have improved in recent series)
#8: Functional MR

- Treat underlying CAD
- Optimal medical treatment
- Cardiac resynchronization therapy
- Role in:
  - ? Bridge to LVAD
  - ? Salvage
- Heart Team discussion
2017 H Baumgartner et al.
...a percutaneous edge-to-edge procedure may be considered...

ERO > 20 mm²  RV > 30 mL

2017 AHA/ACC Focused Update
...The best therapy for chronic secondary MR is not clear because MR is only 1 component of the disease...

ERO > 40 mm²  RV > 60 mL
The MITRA-FR Trial

304 pts with SMR due to LV dysfunction with LVEF 15-40%, NYHA II-IV, HF hospitalization within the prior 12 months

MR defined by EU “severe” criteria as EROA >20 mm² or RVol >30 mL/beat. Both groups with “real-world” HF meds (not maximally-tolerated GDMT)

Randomize 1:1 at 37 French centers

MitraClip + MT  
N=152

MT alone  
N=152

Primary endpoint
Freedom from death or HF hospitalizations through 12 months

MITRA-FR: 12-Month Outcomes

Primary endpoint: Freedom from death or HF hospitalizations

![Graph showing freedom from death or HF hospitalization over time]

<table>
<thead>
<tr>
<th></th>
<th>MitraClip + MT</th>
<th>MT alone</th>
<th>OR [95% CI] or HR [95% CI]*</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>1° EP: Death or HF hosp</td>
<td>54.6%</td>
<td>51.3%</td>
<td>1.16 [0.73–1.84]</td>
<td>0.53</td>
</tr>
<tr>
<td>Death</td>
<td>24.3%</td>
<td>22.4%</td>
<td>1.11 [0.69–1.77]*</td>
<td>0.65</td>
</tr>
<tr>
<td>CV death</td>
<td>21.7%</td>
<td>20.4%</td>
<td>1.09 [0.67–1.78]*</td>
<td>0.74</td>
</tr>
<tr>
<td>HF hosp</td>
<td>48.7%</td>
<td>47.4%</td>
<td>1.13 [0.81–1.56]*</td>
<td>0.59</td>
</tr>
<tr>
<td>MACE*</td>
<td>56.6%</td>
<td>51.3%</td>
<td>1.22 [0.89–1.66]*</td>
<td>–</td>
</tr>
</tbody>
</table>

* MACE = Death, MI, CVA, HF hosp

• FMR 3+ or 4+
• NYHA II-IV despite maximal tolerated GDMT and CRT

Transcatheter Mitral-Valve Repair in Patients with Heart Failure

All HF Hospitalizations
Primary Effectiveness

Cumulative HF Hospitalizations (n)

- MitraClip + GDMT
- GDMT alone

283 in 151 pts
160 in 92 pts

NNT (24 mo) = 3.1 [95% CI 1.9, 8.2]

HR (95% CI) = 0.53 [0.40-0.70]
P<0.001

No. at Risk:
- MitraClip: 302, 286, 269, 253, 236, 191, 178, 161, 124
- GDMT: 312, 294, 271, 245, 219, 176, 145, 121, 88

Time After Randomization (Months)

All-cause Mortality

HR [95% CI] = 0.62 [0.46-0.82]

P<0.001

NNT (24 mo) = 5.9 [95% CI 3.9, 11.7]

No. at Risk:
- MitraClip + GDMT: 302, 286, 269, 253, 236, 191, 178, 161, 124
- GDMT alone: 312, 294, 271, 245, 219, 176, 145, 121, 88
Primary Effectiveness Endpoint
Hospitalizations for HF within 24 months

Annualized rates of HF hospitalization*

NNT (24 mo) = 3.1 [95% CI 1.9, 8.2]

- GDMT alone
  - 283/416.8 pt-yrs
  - 67.9%

- MitraClip + GDMT
  - 160/446.5 pt-yrs
  - 35.8%

HR (95% UCL) = 0.53 [0.66]
P<0.001

*Joint frailty model
Primary Safety Endpoint
Freedom from Device-related Complications within 12 months

96.6%* (95% LCL: 94.8%)

88% OPC

P<0.001

MitralClip procedure attempted
N=293

<table>
<thead>
<tr>
<th>Device-related complications</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Single leaflet device attachment</td>
<td>2</td>
</tr>
<tr>
<td>- Device embolization</td>
<td>1</td>
</tr>
<tr>
<td>- Endocarditis requiring surgery</td>
<td>0</td>
</tr>
<tr>
<td>- Mitral stenosis requiring surgery</td>
<td>0</td>
</tr>
<tr>
<td>- Left ventricular assist device implant</td>
<td>3</td>
</tr>
<tr>
<td>- Heart transplant</td>
<td>2</td>
</tr>
<tr>
<td>- Any device-related complication requiring non-elective CV surgery</td>
<td>1</td>
</tr>
</tbody>
</table>

*KM estimate; **Calculated from Z test with Greenwood's method of estimated variance against a pre-specified objective performance goal of 88%
MITRA-FR vs. COAPT

MITRA-FR

Death or HF Hospitalization (%)

OR [95% CI] = 1.16 [0.73–1.84]  
P=0.53

54.6%  
51.3%

Months

No. at Risk:
Control Group 152  
Device Group 151

MitraClip + MT  
MT alone

COAPT

Death or HF Hospitalization (%)

HR [95% CI] = 0.63 [0.49–0.82]  
P<0.001

46.5%  
33.9%

Months

No. at Risk:
Control Group 312  
Device Group 302

MitraClip + GDMT  
GDMT alone

Obadia JF et al. NEJM. 2018 Aug 27

Stone GW et al. NEJM. 2018 Sept 23.
# Patient selection

## Why are the COAPT Results so Different from MITRA-FR? Possible Reasons

<table>
<thead>
<tr>
<th></th>
<th>MITRA-FR (n=304)</th>
<th>COAPT (n=614)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe MR entry criteria</td>
<td>Severe FMR by EU guidelines: EROA &gt;20 mm² or RV &gt;30 mL/beat</td>
<td>Severe FMR by US guidelines: EROA &gt;30 mm² or RV &gt;45 mL/beat</td>
</tr>
<tr>
<td>EROA (mean ± SD)</td>
<td>31 ± 10 mm²</td>
<td>41 ± 15 mm²</td>
</tr>
<tr>
<td>LVEDV (mean ± SD)</td>
<td>135 ± 35 mL/m²</td>
<td>101 ± 34 mL/m²</td>
</tr>
<tr>
<td>GDMT at baseline and FU</td>
<td>Receiving HF meds at baseline – allowed variable adjustment in each group during follow-up per “real-world” practice</td>
<td>CEC confirmed pts were failing maximally-tolerated GDMT at baseline – few major changes during follow-up</td>
</tr>
<tr>
<td>Acute results: No clip / ≥3+ MR</td>
<td>9% / 9%</td>
<td>5% / 5%</td>
</tr>
<tr>
<td>Procedural complications*</td>
<td>14.6%</td>
<td>8.5%</td>
</tr>
<tr>
<td>12-mo MitraClip ≥3+ MR</td>
<td>17%</td>
<td>5%</td>
</tr>
</tbody>
</table>
The Mortality Benefit of Therapies for HFrEF

- **ACE inhibitor or ARB**: 16%
- **Sacubitril / valsartan**: 32%
- **Beta-blockers**: 36%
- **Mineralocorticoid receptor antagonists**: 28%
- **Isordil / hydralazine**: 28%
- **ICD**: 24%
- **CRT**: 37%
- **MitraClip (COAPT)**: 42%

All class I guideline recommendations
Finding the right patient?

Proportionate vs. Disproportionate MR: A conceptual framework

Disproportionate MR: severe MR out of proportion to underlying

Appropriate MR: not the primary cause of symptoms
Multiparametric Echocardiographic MR Assessment

Secondary MR, Severity 3+ or 4+ (graded by 1 of 3 criteria)

Tier 1
EROA $\geq 0.3 \text{ cm}^2$
or PV systolic flow reversal
N=570 (85.7%)

Tier 2
EROA 0.2 cm$^2$ - $<$0.3 cm$^2$
With any 1 of the following:
- RV $\geq 45 \text{ ml/beat}$
- RF $\geq 40\%$
- VC width $\geq 0.5 \text{ cm}$
N=70 (10.5%)

Tier 3
EROA not measured or $<0.2 \text{ cm}^2$
With at least 2 of the following:
- RV $\geq 45 \text{ ml/beat}$
- RF $\geq 40\%$
- VC width $\geq 0.5 \text{ cm}$
- PISA radius $>0.9 \text{ cm}$, but CW of MR jet not done
- Large ($\geq 6.0 \text{ cm}$) holosystolic jet wrapping around LA
- Peak E velocity $\geq 150 \text{ cm/s}$
N=25 (3.8%)

+ LVEF 20-50% and LVESD $\leq 70 \text{ mm}$
No severe PHTN or RV failure

Asch F. ACC 2019.
#9 Cases done in NHCS

- DMR
- FMR
- HOCM + DMR
Degenerative MR
Case Description

- 75 year old Male
- Severe MR from flail P2
  - Heart failure admissions x 2
  - NYHA II-III
  - LVEF 40-45%. Dilated LV
  - Left and right heart cath: Minor CAD, mPAP 29mmg
- Atrial fibrillation CHADSVASc 3
Heart Team Discussion

- 1st option MV surgery
- However, patient strongly declined surgery and opted for MitraClip
1st Clip

Residual moderate MR lateral to 1st clip
2nd Clip
Final Result

Residual 1+ MR
Post Procedure

• Discharged well after 4 days
• 3 years later
  • NYHA Class I
  • Travelling overseas
  • No further HF admissions
P1 Flail

- 66 year old Male
- Bioprosthetic AVR + CABG x 1, pAF, DM, HTN, HLD
- Recurrent HF admissions
MitraClip x 2
Final 1+ MR
P3 and PM Commissure

- 73 year old Male
- Stage 4 CKD, Calcified aorta, Prostate CA s/p RT, DM, HLD
- Severe MR - P3 and PM commissure flail
MitraClip x 1
Final Trace MR
Torrential P2 DMR

- 59 year old Male
- Cardiogenic shock with multiorgan failure
- Torrential MR from flail P2
Flail P2
Ruptured chords
Salvage MitraClip

MitraClip x 1
Residual mild MR
Mixed DMR and FMR

- 63 year old Male
- Dilated CMP (LVEF 20-25%), AF
- Severe MR
  - Dilated mitral annulus 4.3cm
  - P2 prolapse
- Worsening ET (NYHA II-III)
MitraClip x 2
Residual 1+ MR
Functional MR
FMR
Case 1

- 70 year-old Female
- Ischemic CMP, PCI to LAD/RCA
- ICD for secondary prevention
- NYHA III
- Functional MR – Mod-severe
- LVEF 22%, Dilated LV
- Mitra Clip x 1
- Residual 2+ MR

- 6 years post-procedure
  - NYHA Class II
  - No heart failure hospitalization
FMR Case 2

- 83-year old Male
- Non-ischaemic CMP, Stage 4 CKD
- Cardiogenic shock, IV Dobutamine
- Functional MR – mod-severe, LVEF 25%
• MitraClip x 1
• Residual 1-2+ MR

• Discharge stable and ambulating 4 days post-procedure

• 1 year follow-up
  • NYHA Class I
  • Exercises on bike daily
FMR Case 3
MitraClip in a Patient With Acute Heart Failure Associated With Dynamic Functional MR After Perioperative MI

- 50-year-old Female
- Admitted for mastectomy for breast cancer
- Developed ST depression intra-operatively
- Developed Anterior STEMI and cardiogenic shock in shortly after reaching SICU
- Sent for primary PCI
Shortly After Cathlab Arrival

- VT and PEA
- CPR for 15 minutes
- TPW and IABP implanted
Initial Coronary Angiography

Complete occlusion of LM

Normal Flow RCA
Primary PCI

1 BMS implanted in LM-LAD

Total revascularization, TIMI 2 flow

ECMO implanted
TTE Evaluation post PPCI

LV EF 15-20%
normal LV dimension

Trivial MR
Post Primary PCI

- Improved Hemodynamics - ECMO explanted
- Failed to wean ventilator and IABP for six weeks due to repeated episodes of flash pulmonary edema
- Developed abdominal hematoma (evacuated)
TTE and TEE After ECMO Explantation

LVEF 25-30% - On Inotropes and IABP Support

Tenting of MV leaflets
Moderate MR

Systolic Blunting of PV Flow

Increased coaptation height
TEE With Inotrope Challenge

Systolic BP 82 mmHg
PASP 47 mmHg

Systolic BP 130 mmHg
PASP 79 mmHg

Dynamic MR from moderate to severe with increasing BP
Regurgitation jet arising from A2/P2 coaptation site
At rest and sedated

Started dopamine
Percutaneous Mitral Valve Repair Decision

• Discussed with cardiac surgical team
• Very high surgical risk - STS Risk Score: 68% mortality, 82% morbidity / mortality
• Family was not keen for surgery
• Decided for percutaneous mitral valve repair
Angiography Pre MitraClip
MitraClip Procedure

Post 1st Clip implant:
Residual Jet lateral to clip

Post 2nd Clip implant:
Mild MR - in between & lateral to clip
MitraClip Result
Acceptable post MC mean gradient 5 mmHg
Improved PV flow pattern from systolic blunting to systolic predominance
Post MitraClip Implantation

- Patient made gradual recovery
- No more episodes of pulmonary edema
- Weaned off mechanical ventilator and IABP
- Eventually was discharged
5 Months Evaluation After MitraClip

LV Dimension mildly enlarged, LVEF 25%, mild-mod MR
Patient stable in NYHA class II

Clips were stable in position
Residual mild-moderate MR medial and lateral to clips
2 years later
2 year later
HOCM + DMR

KILLING 2 BIRDS WITH ONE STONE:
MITRACLIP IN SYSTOLIC ANTERIOR
MOTION OF MITRAL VALVE AND FLAIL P2
Case Description

- 76-year-old, female
- Past medical history
  - Obstructive Hypertrophic Cardiomyopathy (HOCM)
  - Atrial fibrillation on Rivaroxaban
  - Cerebrovascular accident 2013
  - Rectal adenocarcinoma underwent surgical resection 2011
- 5 admissions in 2 months for dyspnea and angina at rest and on exertion
- Medications: Verapamil 240mg OD, Bisoprolol 2.5mg OD
- Coronary angiogram: minor disease
Transthoracic Echocardiogram

HCM + SAM

SAM + MR

SAM

Flail P2

LVOT PPG
76mmHg
Transesophageal Echocardiogram

Flail P2

SAM and MR

SAM and MR

3D Color
Heart Team Discussion

• The recent deterioration was predominantly contributed by the new development of the flail P2, resulting in severe symptomatic MR, instead of HOCM
• Medical management difficult due to the effect of diuresis on LVOT obstruction, and resultant angina
• Surgical management complicated in view of double valve replacement (moderate aortic regurgitation and small LVOT)
• Decision was made for MitraClip procedure
MitraClip Procedure – 1st Clip

- 1st clip placed centrally over flail segment
- Reduction of MR grade from 4+ to 2+
- Residual MR at A1 segment and lateral to 1st clip
- The residual MR jet is posteriorly directed (SAM-related MR)
Decision for 2\textsuperscript{nd} Clip

- Initial difficulty grasping the anterior mitral valve leaflet
- Eventually, 2\textsuperscript{nd} clip successfully deployed with reduction of MR to 1-2+
Progress

• In addition, there was reduction in SAM and LVOT peak pressure gradient

• Blood pressure improved significantly post procedure from 90mmHg to 160mmHg

• Discharged well with symptomatic improvement

• 1 month TTE showed stable clips, MR 2+ and LVOT PPG at 38 mmHg
Aortic stenosis: TAVR updates
Outline

• Aortic stenosis: pathology & clinical features
• Diagnosis, investigation and prognosis
• Treatment options
• Updates for TAVI
  • Indications for TAVI vs surgery
    • Moderate surgical risk patients
    • Low surgical risk patients
  • TAVI for failing bioprosthetic surgical valves
  • Embolic protection
• Centrepiece of the heart
• Close association with anterior mitral valve leaflet and inter-ventricular septum, AV node.
Aortic Stenosis Causes

- Congenital
  - Bicuspid AV
  - Supra-valvular obstruction (30-50% have Williams syndrome)
  - Sub-valvular obstruction

- Acquired
  - Degenerative tricuspid AV
  - Degenerative bicuspid AV
  - Rheumatic Heart disease
### Severity of aortic stenosis

<table>
<thead>
<tr>
<th></th>
<th>Aortic jet velocity (m/sec)</th>
<th>Mean gradient (mmHg)</th>
<th>Valve area (cm²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>≤2.0</td>
<td>&lt;5</td>
<td>3.0 to 4.0</td>
</tr>
<tr>
<td>Mild</td>
<td>&lt;3.0</td>
<td>&lt;25</td>
<td>&gt;1.5</td>
</tr>
<tr>
<td>Moderate</td>
<td>3.0 to 4.0</td>
<td>25 to 40</td>
<td>1.0 to 1.5</td>
</tr>
<tr>
<td><strong>Severe</strong></td>
<td><strong>&gt;4.0</strong></td>
<td><strong>&gt;40</strong></td>
<td><strong>&lt;1.0</strong></td>
</tr>
</tbody>
</table>
AS: Clinical presentation

• Classical symptoms are:
  • Angina
  • Syncope
  • Dyspnea (heart failure)
Treatment

• Medical therapy
• Balloon aortic valvuloplasty
• Aortic valve replacement
  • Surgical AVR
    • Mechanical
    • Bioprosthetic
  • Transcatheter AVR
Medical therapy

- Only effective therapy for severe AS is valve replacement
- Medical therapy options are of marginal benefit
- No medical therapies proven to delay progression of AS including statins
- No need for antibiotic prophylaxis
- Avoidance of competitive sports

Does not work once symptomatic
Balloon Aortic Valvuloplasty

• Mainly indicated for young adults with bicuspid AV.
Balloon Aortic Valvuloplasty

- Limited application for degenerative AS
- Risky: up to 20%
- Complications: CVA, bleeding, worsening AR, aortic root disruption
- Restenosis within 6 months

Palliative
Surgical Aortic Valve replacement

- **Gold standard** for treatment of Aortic stenosis
- Restores survival of AS patients back to age matched population
TAVI in 2019
Self-Expanding and Balloon-Expandable Clinical Trials

Clinical Trials with self-expanding and balloon-expandable TAVI devices have demonstrated excellent safety and device success in extreme, high, and intermediate surgical risk patients
Patient Selection
AHA/ACC and ESC/EACTS Guideline Recommendations

The AHA/ACC and ESC/EACTS Guidelines for the Management of Patients with Valvular Heart Disease were updated 2017 to reflect these results:

SAVR is recommended in patients at low-risk while TAVI is now a Class I indication for high-risk patients, with the choice left to the Heart Team for intermediate-risk patients based on individual patient characteristics.
Patient Selection
Intermediate- and High-Risk Patients

In addition to risk scores, the guidelines also provide clinical characteristics, anatomical and technical aspects, and cardiac conditions that can guide patients towards TAVI or SAVR.

<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>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>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Anatomical and technical aspects</th>
<th>Favours TAVI</th>
<th>Favours SAVR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Favourable access for transfemoral TAVI</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Unfavourable access (any) for TAVI</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Sequence of chest radiation</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Porcelain aorta</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Presence of intact coronary bypass grafts at risk when sternotomy is performed</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Expected patient–prosthesis mismatch</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Severe chest deformation or scoliosis</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Short distance between coronary ostia and aortic valve annulus</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Size of aortic valve annulus out of range for TAVI</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Aortic root morphology unfavourable for TAVI</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Valve morphology (bicuspid, degree of calcification, calcification pattern) unfavourable for TAVI</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Presence of thrombi in aorta or LV</td>
<td>+</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cardiac conditions in addition to aortic stenosis that require consideration for concomitant intervention</th>
<th>Favours TAVI</th>
<th>Favours SAVR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe CAD requiring revascularization by CABG</td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Severe primary mitral valve disease, which could be treated surgically</td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Severe tricuspid valve disease</td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Aneurysm of the ascending aorta</td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Septal hypertrophy requiring myectomy</td>
<td></td>
<td>+</td>
</tr>
</tbody>
</table>

Falk et al., Eur Heart J. 2017 Sep 21;38(36):2739-2791
**Patient and Device Selection in 2019**

*Shift in Focus*

Device selection in these younger patients will be driven by **valve durability** and **performance** of TAVI valves, **lifetime management** of patients, and getting patients back to their daily lives faster.

**TAVR**

- **High Risk Patients**
  - Mortality
  - Morbidity
  - Quality of Life

- **Low Risk Patients**
  - Valve Durability and Performance
  - Lifetime Management
  - Return to Daily Life

**Focus**
Transfemoral Sapien XT

Balloon Inflation
Sapien XT
Sapien Valve Positioning
Valve deployment
Post deployment
TAVI TRIALS: Extreme/high risk
Extreme risk
STS >11
Medical Rx vs TAVI

High risk
STS >8
Surgical AVR vs TAVI
Current TAVI Devices

Problems with early generation devices

• Paravalvular leak
• Inaccurate positioning/Inability to reposition
  • Coronary artery occlusion
  • Paravalvular leak
  • Implant embolization
  • AV block
• Unsuitable Patient Anatomy
  • Low coronary artery height
  • Inadequate femoral-iliac diameter
• Need for aortic annular calcifications to anchor
• Rather large devices with possible vascular injuries
  • Need at least 5mm-6mm femoral iliac arteries for transfemoral TAVI cases
Major TAVR complications

TAVI in 2019
Reducing Complications

Data from clinical trials and registries have demonstrated that device modifications, increased operator experience, better patient selection, and optimized pre-procedural planning have led to a substantial reduction in complications.

Rates of the “Big 5” complications (stroke, paravalvular leak (PVL), acute kidney injury, conduction abnormalities, and major vascular and bleeding complications) have been greatly reduced.
Paravalvular leak

Calcium
- Too High
- Too Low

Heavily calcified cusp

Too Small
LBBB/CHB with TAVI
Coronary artery occlusion
New TAVI Devices
Edwards SAPIEN 3 THV

Low Frame Height
- Respects the cardiac anatomy

Bovine Pericardial Tissue
- Scalloped leaflet shape
- Carpentier-Edwards ThermaFix* process is intended to minimize the risk of calcification

Inner Skirt
- Polyethylene terephthalate (PET)

Outer Skirt
- PET outer skirt designed to minimize paravalvular leak

*No clinical data are available which evaluate the long-term impact of the Carpentier-Edwards ThermaFix process in patients
Lotus Valve

- Nitinol Frame
- Adaptive Seal
- Locking Mechanism
- Bovine Pericardium

Release Mechanism
Unsheath, Lock
Unlock, Resheath
CoreValve Evolute R – Key Improvements

• 14F Sheath Compatible
• 1:1 response
• Self Centering
• Repositionable
• Retrievable
UPDATES ON TAVI

• Indications for TAVI vs surgery
  • Moderate surgical risk patients
  • Low surgical risk patients
• TAVI for failing bioprosthetic surgical valves
• Embolic protection
• 2032 intermediate-risk patients (STS 4-8)
• Severe aortic stenosis,
• 57 centers
• TAVR (balloon expandable Edwards TAVI vs surgical replacement)
• TAVR group 73% Transfemoral access, 27% transapical
• Primary end point was death or stroke at 2 years.
Overall TAVI vs SAVR no difference in primary end point

TF TAVI vs SAVR: reduced primary end point
Surgical or Transcatheter Aortic-Valve Replacement in Intermediate-Risk Patients


- 1746 patients
- 87 centers.
- TAVI using Self-expanding Corevalve vs SAVR
- Mean STS score: 4.5%
**Surgery:**
- higher rates of acute kidney injury,
- More atrial fibrillation,
- More blood transfusion

**TAVR:**
- More aortic regurgitation
- More need for pacemaker implantation.
- Lower mean gradients
- Larger aortic-valve areas
• 1000 patients TAVR vs SAVR
• mean 73 years
• mean STS risk score was 1.9%
• primary end point (death/CVA/rehospitalisation 1 year) lower in the TAVR group
• (8.5% vs. 15.1%; P<0.001 for noninferiority;
• TAVR resulted in less
  • Death or stroke (P = 0.01)
  • new-onset atrial fibrillation (P<0.001).
  • Hospitalization duration
• No differences in major vascular complications, new permanent pacemaker insertions, or moderate or severe paravalvular regurgitation.
Patient Selection
Low Risk TAVI | PARTNER 3

The PARTNER 3 trial found TAVI with Sapien 3 had significantly less death, stroke, or rehospitalization out to 1 year.

The Evolut Low-Risk and PARTNER 3 data will likely drive an indication in 2019 for treating low surgical risk patients!

Age, rather than risk, will be key in selecting patients for TAVI.
1403 patients. TAVI vs SAVR
mean age 74 years.
24-month (death/CVA) primary end point was 5.3% in the TAVR group and 6.7% in SAVR
TAVR, vs SAVR
Less disabling stroke (0.5% vs. 1.7%),
Less bleeding complications (2.4% vs. 7.5%),
Less acute kidney injury (0.9% vs. 2.8%), and
Less AF (7.7% vs. 35.4)
More PPM(17.4% vs. 6.1%).
TAVI group has better valvular hemodynamics at 12 months
Patient Selection
Low Risk TAVI | Evolut Low Risk

Results from the randomized Evolut Low-Risk Trial demonstrated significantly less death, disabling stroke, or HF hospitalization out to 1 year compared to surgery.
TAVR can be considered an alternative treatment for low-risk patients

**PARTNER 3**

**Evolute Low Risk Trial**

- **Hazard ratio, 0.54 (95% CI, 0.37–0.79)**
  - *P* = 0.001 by log-rank test

---

**Death, Stroke, or Rehospitalization (%)**

- **Surgery**
  - Months since Procedure:
    - 0: 4.2
    - 3: 8.5
    - 6: 15.1
- **TAVR**
  - Months since Procedure:
    - 0: 4.2
    - 3: 8.5
    - 6: 15.1

**No. at Risk**

- **Surgery**
  - 0: 454
  - 3: 408
  - 6: 390
  - 9: 381
  - 12: 377
  - 15: 374

- **TAVR**
  - 0: 496
  - 3: 475
  - 6: 467
  - 9: 462
  - 12: 456
  - 15: 451

---

- **Death or Disabling Stroke (%)**

- **Surgery**
  - Months:
    - 0: 4.2
    - 6: 2.7
    - 12: 2.2
    - 18: 1.8
    - 24: 1.5

- **TAVR**
  - Months:
    - 0: 4.2
    - 6: 3.5
    - 12: 2.9
    - 18: 2.4
    - 24: 2.0

**No. at Risk**

- **Surgery**
  - 0: 678
  - 6: 576
  - 12: 366
  - 18: 195
  - 24: 69

- **TAVR**
  - 0: 725
  - 6: 648
  - 12: 435
  - 18: 233
  - 24: 80

---

Cerebral Embolic protection devices
Protection Against Cerebral Embolism During Transcatheter Aortic Valve Replacement

Samir R. Kapadia, MD, Susheel Kodali, MD, Raj Makkar, MD, Roxana Mehran, MD, Ronald M. Lazar, PhD, Robert Zivadinov, MD, PhD, Michael G. Dwyer, MD, Hasan Jilaihawi, MD, Renu Virmani, MD, Salf Anwaruddin, MD, Vinod H. Thourani, MD, Tamim Nazif, MD, Norman Mangner, MD, Felix Wolte, MD, Amar Krishnaswamy, MD, Stephanie Mick, MD, Tarun Chakravarty, MD, Mamoo Nakamura, MD, James M. McCabe, MD, Lowell Satler, MD, Alan Zajarias, MD, Wilson Y. Szeto, MD, Lars Svensson, MD, PhD, Maria C. Ahu, MS, Roseann M. White, MA, Carlye Kraemer, MS, Azin Parhizgar, PhD, Martin B. Leon, MD, Axel Linke, MD, on behalf of the SENTINEL Trial Investigators

- 363 patients undergoing TF TAVI
- Cerebral protection vs control
- MACCE no difference.
- New lesion volume was 178.0 mm³ in control subjects and 102.8 mm³ in the device arm (p = 0.33).
- Strokes at 30 days were 9.1% in control subjects and 5.6% in patients with devices (p = 0.25)
TAVI for failing bioprosthetic surgical valves
Surgically Implanted Bioprosthetic Valve: Summary

Disadvantages: Limited durability beyond 10 years especially in younger patients: cusp degeneration or tears, Ca\(^{++}\), pannus formation and endocarditis (1–4% of patients during the 1st year, and in approximately 1% per year thereafter.)

![Images of tears, calcification, and infective endocarditis]

![Image of Pannus and Thrombus]

Freedom from Event (Severe AS/AR or Redo)

• 459 patients
• 55 centers
• At 1 month
  • 35 (7.6%) patients died, 8 (1.7%) had major stroke,
  • 313 (92.6%) of surviving patients NYHA I-II
  • 1 year survival rate was 83.2%
Structural and procedural difference between TAVR and SAVR valve

Micro CT

- Thinner leaflets for transcatheter delivery (TAVR 0.25mm, SAVR 0.4 mm)
- Native aortic valve calcification and oval-shaped annulus hamper circular and symmetric stent deployment
- Higher stress and strain are burdened into a prosthesis during procedure

Hwang IC et al. Circ J. 2019 Apr 5. [Epub ahead of print]

Long-term durability is not the same?
Long term f/u of TAVR NOTION Trial 6-year f/u

- Structural Valve Deterioration (SVD)
- Bioprosthetic Valve Failure (BVF)

BVF (Valve-related Death, AV reintervention, severe SVD) rate were low and similar for both groups

PPM rates

Lifetime Management
Permanent Pacemaker Implantation

- New conduction abnormalities after TAVI have been associated with poor outcomes and increased risk of permanent pacemaker implantation. Choosing a valve that reduces the risk of new conduction abnormalities will be critical for the lifetime management of TAVI patients.

- Studies have found that balloon-expandable valves have the lowest permanent pacemaker rates, and mechanically expanding the highest.
Younger patients requiring PCI

TAVR Device Selection
Post-TAVI PCI Current State

A recent review provided risk factors and guidelines for how to access the coronary arteries post-TAVI with CoreValve and Sapien

- The review suggested that post-TAVI PCI is a TAVI problem
- Patients with narrow sinuses, low coronaries, and small sinotubular junctions are at increased risk with all TAVI devices

Yudi, et al., J Am Coll Cardiol 2018; 71(12):1360–78
GALILEO Trial

GALILEO (Global multicenter, open-label, randomized, event-driven, active-controlled study comparing a rivaroxaban-based antithrombotic strategy to an antiplatelet-based strategy after transcatheter aortic valve replacement (TAVR) to optimize clinical outcomes will compare rivaroxaban-based)

1520 patients after successful TAVI procedure

Rivaroxaban 10 mg OD and Aspirin 75-100 mg OD

Rivaroxaban 10 mg OD

Clopidogrel 75 mg OD Aspirin 75-100 mg OD

Aspirin 75-100 mg OD

Drop of aspirin

Drop of clopid

Primary end-point is death, MI, stroke, non-CNS systemic emboli, symptomatic valve thrombosis, deep vein thrombosis or pulmonary embolism, major bleedings over 720 days of treatment exposure.
Ongoing Trials : ATLANTIS

ATLANTIS (Anti-Thrombotic Strategy to Lower All cardiovascular and Neurologic Ischemic and Hemorrhagic Events after Trans-Aortic Valve Implantation for Aortic Stenosis)

1509 patients after successful TAVI procedure

Stratum 1
Indication for OAT

Stratum 2
No indication for OAT

R:1:1

VKA

Apixaban 5mg bid*

DAPT/SAPT

Primary end-point is a composite of death, MI, stroke, systemic emboli, intracardiac or bioprosthesis thrombus, episode of deep vein thrombosis or pulmonary embolism, major bleedings over one year follow-up.

*2.5mg bid if creatinine clearance 15-29ml/min or if two of the following criteria: age≥80 years, weight≥60kg or creatinine≥1.5mg/dl (133μMol).
**ENVISAGE Trial – Current Status ~700 pts**

Pls: G. Dangas, N. vanMiegheem

---

**Successful TAVR n=1400**

Patients *With an Indication to Chronic Oral Anticoagulation*

- **Randomize 1:1**
  - 1-7 Days after the procedure
  - Background Tx: Single Antiplatelet Therapy as per treating MD discretion (*Stratification Variable*)

- **Warfarin (target INR 2-3)**

- **EDOXABAN 60mg po daily**
  - Adjustment to 30mg for low eGFR etc

- Minimum duration of randomized therapy 12 months

- **Clinical Follow-up: 1, 6, 12 Months**

---

**Secondary Endpoints**

- All-cause Death, MI, Stroke or TIA, VARC-2 Life-threatening (LT) bleeding and Major bleeding

---

**Primary Safety Endpoint:**

- Major Bleeding

---

**Primary Endpoint - NACE**

- [Composite of Death, MI, Stroke, TIA, systemic thromboembolism or VARC-2 Life-threatening (LT) or Major bleeding]

---

**Ancillary Studies**

- Cost-Effectiveness
- QoL substudy
Age is the main determinant

Possible Strategies According to Age

<table>
<thead>
<tr>
<th>Age Range</th>
<th>Treatment Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 80 y</td>
<td>V-in-V</td>
</tr>
<tr>
<td>80-84 y</td>
<td>V-in-V</td>
</tr>
<tr>
<td>75-79 y</td>
<td>SAVR or V-in-V (age)</td>
</tr>
<tr>
<td>70-74 y</td>
<td>SAVR If SVD: V-in-V</td>
</tr>
<tr>
<td>65-69 y</td>
<td>?</td>
</tr>
<tr>
<td>&lt; 65 y</td>
<td>Redo- SAVR or V-in-V</td>
</tr>
</tbody>
</table>

SVD at 5 y

SVD at 10 y

Heart Team and patient discussion
Summary

• TAVI has been established as alternative for treatment of aortic stenosis in high risk patients
• Promising evidence in low to moderate risk
• Improvements in Device designs will in future improve patients’ outcome
• Long Term durability ?
• SAVR will remain the best option for patients who are not optimal candidates for TAVR, and for the youngest patients
Thank you!