Percutaneous Treatment of Valvular Heart Diseases: Lessons and Perspectives

Bernard Iung
Bichat Hospital, Paris
Euro Heart Survey on Valvular Diseases

3547 Patients with Native Valve Disease

(Iung et al. Eur Heart J 2003;24:1244-53)
Closed-heart commissurotomy  Open-heart commissurotomy

Percutaneous mitral commissurotomy: K.Inoue 1984
## Late Results after PMC

<table>
<thead>
<tr>
<th>Study</th>
<th>n=</th>
<th>Age (yrs)</th>
<th>FU (yrs)</th>
<th>% Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cohen (NEJM 1992)</td>
<td>146</td>
<td>59</td>
<td>5</td>
<td>51**</td>
</tr>
<tr>
<td>Orrange (Circulation 1997)</td>
<td>132</td>
<td>44</td>
<td>7</td>
<td>65**</td>
</tr>
<tr>
<td>Ben Farhat (Circulation 1998)</td>
<td>30</td>
<td>29</td>
<td>7</td>
<td>90*</td>
</tr>
<tr>
<td>Meneveau (Heart 1998)</td>
<td>532</td>
<td>54</td>
<td>7,5</td>
<td>52*</td>
</tr>
<tr>
<td>Stefanadis (JACC 1998)</td>
<td>441</td>
<td>44</td>
<td>9</td>
<td>75*</td>
</tr>
<tr>
<td>Hernandez (Circulation 1999)</td>
<td>561</td>
<td>53</td>
<td>7</td>
<td>69*</td>
</tr>
<tr>
<td>Iung (Circulation 1999)</td>
<td>1024</td>
<td>49</td>
<td>10</td>
<td>56**</td>
</tr>
<tr>
<td>Palacios (Circulation 2002)</td>
<td>879</td>
<td>55</td>
<td>12</td>
<td>33**</td>
</tr>
</tbody>
</table>

(*: Survival without intervention  **: Survival without intervention and NYHA I / II)
Management of Severe Symptomatic Mitral Stenosis

- Symptomatic MS < 1.5 cm²
  - CI to PMC
  - CI or high risk for surgery
    - Yes
      - CI to PMC
    - No
      - Favourable anatomical characteristics
        - Favourable clinical characteristics
          - PMC
        - Unfavourable clinical characteristics
          - Surgery
      - Unfavourable anatomical characteristics
        - Surgery

© 2007 European Society of Cardiology
Type of Intervention
Native Valve Disease

N= 512  119  112  155

- Percut. Int.
- Valve Repair
- Bioprosthesis
- Mech Prosthesis
- Homograft
- Autograft

European Society of Cardiology – Euro Heart Survey
PMC Across the Five Continents

Papeete, Boston, Sao Paulo, Paris, Monastir, Maputo, Ho Chi Minh City

(Marijon et al. Arch Cardiovasc Dis 2008;101:611-7)
## PMC Worldwide: Results

<table>
<thead>
<tr>
<th></th>
<th>Non-Western countries (n=250)</th>
<th>Western countries (n=100)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>In-hospital cardiac death (%)</td>
<td>0.8</td>
<td>1.0</td>
<td>0.85</td>
</tr>
<tr>
<td>Mitral regurgitation ≥ 3/4</td>
<td>2.8</td>
<td>5.0</td>
<td>0.31</td>
</tr>
<tr>
<td>Embolism (%)</td>
<td>0.8</td>
<td>2.0</td>
<td>0.21</td>
</tr>
<tr>
<td>Cardiac tamponade (%)</td>
<td>1.6</td>
<td>0.0</td>
<td>0.47</td>
</tr>
<tr>
<td>Surgery &lt; 30 days (%)</td>
<td>3.2</td>
<td>4.0</td>
<td>0.71</td>
</tr>
<tr>
<td>Final valve area (cm²)</td>
<td>1.91 ± 0.36</td>
<td>1.84 ± 0.46</td>
<td>0.14</td>
</tr>
<tr>
<td>Final indexed valve area (cm²/m² BSA)</td>
<td>1.22 ± 0.27</td>
<td>1.08 ± 0.29</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Good Immediate Results</td>
<td>90</td>
<td>88</td>
<td>0.53</td>
</tr>
</tbody>
</table>

(Marijon et al. Arch Cardiovasc Dis 2008;101:611-7)
Aortic Stenosis

INSERM  Bichat
Severe Symptomatic AS in the Elderly

Severe AS: Valve Area ≤ 0.6 cm²/m² BSA or Mean Gradient ≥ 50 mmHg
Symptomatic AS: NYHA Class III or IV or Angina

(Aungh et al. Eur Heart J 2005;26:2714-20)
Percutaneous Aortic Valve Implantation

Edwards Sapien™

Medtronic CoreValve™

Right Subclavian

Left Subclavian

Transapical

Transfemoral (22-24 Fr.)

Transfemoral (18 Fr.)
Transfemoral Aortic Valve Implantation

Edwards Sapien  Medtronic CoreValve
# Transfemoral Aortic Valve Implantation

## Population

<table>
<thead>
<tr>
<th></th>
<th>Edwards Sapien</th>
<th>Medtronic CoreValve</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Webb et al.</strong></td>
<td>113</td>
<td>136</td>
</tr>
<tr>
<td><strong>Bichat</strong></td>
<td>100</td>
<td>1483</td>
</tr>
<tr>
<td><strong>Source</strong></td>
<td>463</td>
<td>Post CE 18Fr</td>
</tr>
</tbody>
</table>

| n=                     | 113            | 136                 |
| Age (yr)               | 85             | 81                  |
| Logistic Euroscore (%) | 25             | 23                  |
| AVA (cm²)              | 0.6            | 0.6                 |

(* Including 15 cases with Medtronic CoreValve)

## Transfemoral Aortic Valve Implantation
### 30-Day Results

<table>
<thead>
<tr>
<th></th>
<th>Edwards Sapien</th>
<th>Medtronic CoreValve</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><em>Webb et al.</em></td>
<td><em>Bichat</em></td>
</tr>
<tr>
<td>(%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Implant success</td>
<td>94</td>
<td>94</td>
</tr>
<tr>
<td>Death</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Neurological complic.</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Permanent pacemaker</td>
<td>4</td>
<td>12</td>
</tr>
<tr>
<td>Vascular complications</td>
<td>8</td>
<td>12</td>
</tr>
<tr>
<td>AR &gt; 2/4</td>
<td>5</td>
<td>3</td>
</tr>
</tbody>
</table>

(* Including 15 cases with Medtronic CoreValve)
Transfemoral Aortic Valve Implantation

Survival

Edwards Sapien (n=113)

Medtronic CoreValve (n=175)

Transfemoral Aortic Valve Implantation
Functional Results

Symptoms
1-year NYHA class

Quality of life
Health concepts derived from SF-12


(Ussia et al. Eur Heart J 2009;30:1790-6)
Transapical Aortic Valve Implantation
# Transapical Aortic Valve Implantation

<table>
<thead>
<tr>
<th></th>
<th>Leipzig (n=161)</th>
<th>Bichat (n=31)</th>
<th>US registry (n=40)</th>
<th>Partner EU (n=67)</th>
<th>Source (n=575)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (yr)</strong></td>
<td>83</td>
<td>82</td>
<td>84</td>
<td>83</td>
<td>81</td>
</tr>
<tr>
<td><strong>Logistic Euroscore (%)</strong></td>
<td>30</td>
<td>28</td>
<td>36</td>
<td>34</td>
<td>29</td>
</tr>
<tr>
<td><strong>Procedural success (%)</strong></td>
<td>95</td>
<td>100</td>
<td>88</td>
<td>96</td>
<td>93</td>
</tr>
<tr>
<td><strong>Surgical conversion (%)</strong></td>
<td>2.5</td>
<td>0</td>
<td>12</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td><strong>Stroke (%)</strong></td>
<td>0</td>
<td>0</td>
<td>6</td>
<td>0.5</td>
<td>3</td>
</tr>
<tr>
<td><strong>30-day mortality (%)</strong></td>
<td>9.4</td>
<td>13</td>
<td>18</td>
<td>18</td>
<td>10</td>
</tr>
<tr>
<td><strong>6-month survival (%)</strong></td>
<td>76</td>
<td>76</td>
<td>60</td>
<td>55</td>
<td>-</td>
</tr>
</tbody>
</table>
Transcatheter Aortic Valve Implantation

Survival

<table>
<thead>
<tr>
<th>Procedure Type</th>
<th>HR [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early vs. late</td>
<td>3.4 [1.4-8.0]</td>
</tr>
<tr>
<td>Transapical vs. TF</td>
<td>2.2 [0.9-5.2]</td>
</tr>
<tr>
<td>Euroscore</td>
<td>1.006 [0.94-1.04]</td>
</tr>
<tr>
<td>Renal failure</td>
<td>3.5 [1.8-6.8]</td>
</tr>
<tr>
<td>Transapical vs. TF</td>
<td>1.85 [0.99-3.43]</td>
</tr>
</tbody>
</table>

Transcatheter Aortic Valve Implantation

Survival

• 345 procedures in 339 patients (6 centres)
• 30-day mortality 10.4%

Predictors of late mortality
- procedural sepsis
- hemodynamic support
- pulmonary hypertension
- chronic kidney disease
- COPD

(Rodés-Cabau et al. J Am Coll Cardiol 2010;55,in press)
Transcatheter valve implantation for patients with aortic stenosis: a position statement from the European Association of Cardio-Thoracic Surgery (EACTS) and the European Society of Cardiology (ESC), in collaboration with the European Association of Percutaneous Cardiovascular Interventions (EAPCI)

Alec Vahanian\textsuperscript{1*}, Ottavio Alfieri\textsuperscript{2*}, Nawwar Al-Attar\textsuperscript{1}, Manuel Antunes\textsuperscript{3}, Jeroen Bax\textsuperscript{4}, Bertrand Cormier\textsuperscript{5}, Alain Cribier\textsuperscript{6}, Peter De Jaegere\textsuperscript{7}, Gerard Fournia\textsuperscript{9}, Arie Pieter Kappetein\textsuperscript{7}, Jan Kovac\textsuperscript{9}, Susanne Ludgate\textsuperscript{10}, Francesco Maisano\textsuperscript{2}, Neil Moat\textsuperscript{11}, Friedrich Mohr\textsuperscript{12}, Patrick Nataf\textsuperscript{1}, Luc Piérard\textsuperscript{13}, José Luis Pomar\textsuperscript{14}, Joachim Schofer\textsuperscript{15}, Pilar Tornos\textsuperscript{16}, Murat Tuzcu\textsuperscript{17}, Ben van Hout\textsuperscript{18}, Ludwig K. Von Segesser\textsuperscript{19}, and Thomas Walther\textsuperscript{12}

\textsuperscript{1} Hôpital Bichat, Paris, France; \textsuperscript{2} Ospedale San Raffaele, Milan, Italy; \textsuperscript{3} University Hospital, Coimbra, Portugal; \textsuperscript{4} Leiden University Medical Center, Leiden, The Netherlands; \textsuperscript{5} Institut Hospitalier Jacques Cartier, Maisy, France; \textsuperscript{6} CHU de Rouen—Hôpitaux de Rouen—Hôpital Charles Nicolle, Rouen Cedex, France; \textsuperscript{7} Thoraccenter, Erasmus Medical Center, Rotterdam, Netherlands; \textsuperscript{8} CHU—Centre Hospitalier de Rangueil, Toulouse, France; \textsuperscript{9} University Hospitals of Leicester, Leicestershire, UK; \textsuperscript{10} Department of Health, Medicines and Healthcare Products Regulatory Agency, London, UK; \textsuperscript{11} Royal Brompton Hospital, London, UK; \textsuperscript{12} Heart Center Leipzig, University of Leipzig, Leipzig, Germany; \textsuperscript{13} University Hospital Sart Tilman, Liège, Belgium; \textsuperscript{14} Hospital Clinic de Barcelona, University of Barcelona, Barcelona, Spain; \textsuperscript{15} Hannover University Cardiovascular Center, Hannover, Germany; \textsuperscript{16} Hospital Universitari Vall d’Hebron, Barcelona, Spain; \textsuperscript{17} Cleveland Clinic, Cleveland, Ohio, USA; \textsuperscript{18} Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, The Netherlands; and \textsuperscript{19} CHUV, Lausanne, Switzerland

Received 2 April 2008; accepted 10 April 2008, online publish-ahead-of-print 13 May 2008

Aims
To critically review the available transcatheter aortic valve implantation techniques and their results, as well as propose recommendations for their use and development.
« The Team Approach »

Surgeons

Cardiologists

Anesthesiologists

Imaging specialists (Echo, CT, MRI)

Transcatheter Aortic Valve Implantation

With expertise in the treatment of valve disease

(EACTS/ESC/EAPCI Position Statement)
Screening - Vascular imaging
Measurement of Aortic Annulus

Distance Annulus /Coronary Ostia

5.9 mm (2D)

12.6 mm (2D)
How to Decrease the Incidence of Significant AR after TAVI?

Prosthesis-Annulus Cover Index = \frac{(prosthesis diameter - TEE annulus diameter)}{prosthesis diameter}

(Detaint et al. JACC Cardiovasc Interv 2009;2:821-7)
## Screening High-Risk Patients with AS

### Current Status

<table>
<thead>
<tr>
<th>City</th>
<th>n=</th>
<th>TAVI (%)</th>
<th>AVR (%)</th>
<th>Med. Therapy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dallas</td>
<td>71</td>
<td>21</td>
<td>14</td>
<td>65</td>
</tr>
<tr>
<td>Rotterdam</td>
<td>77</td>
<td>18</td>
<td>14</td>
<td>68</td>
</tr>
<tr>
<td>Cleveland</td>
<td>92</td>
<td>20</td>
<td>21</td>
<td>59</td>
</tr>
<tr>
<td>Vancouver</td>
<td>112</td>
<td>43</td>
<td>18</td>
<td>39</td>
</tr>
<tr>
<td>Milano</td>
<td>220</td>
<td>45</td>
<td>14</td>
<td>41</td>
</tr>
<tr>
<td>Paris</td>
<td>230</td>
<td>52</td>
<td>14</td>
<td>34</td>
</tr>
</tbody>
</table>
Indications for TAVI
Future Perspectives

- Technical improvements
  - Smaller and larger versions of existing prostheses
  - Decrease in introducer size
  - New devices

- Imaging: patient selection, guidance of the procedure

- Extension of indications
  - Primary deterioration of bioprosthesis
  - TAVI in patients at low(er) risk for surgical AVR
    - Durability
    - Comparative evaluation (randomised trials)

- Identification of patients who are not candidates to any intervention (poor expected life expectancy / QoL)
  - Risk-benefit (natural history vs. results of interventions)
  - Adapted scores (functional evaluation, psychometric variables…)
The PARTNER US Trial

Population: High Risk/Non-Operable Symptomatic, Critical Calcific Aortic Stenosis

n= up to 690 pts

Cohort A

ASSESSMENT: Operability

Yes

Cohort A TF Powered Independently

1:1 Randomization

Transfemoral vs AVR Control

Primary Endpoint: All Cause Mortality (Non-inferiority)

No

1:1 Randomization

Transapical vs AVR Control

Cohort A TA Powered to be Pooled with TF

Total n= 1040

ASSESSMENT: Operability

No

Cohort B

n=350 pts

ASSESSMENT: Transfemoral Access

Yes

Cohort B

1:1 Randomization

Transfemoral vs Medical Management Control

Primary Endpoint: All Cause Mortality (Superiority)

No

Not in Study
Rationale for the Correction of Ischaemic / Functional MR

(Levine et al. Curr Cardiol Rep 2002;4:125-9)
### Indications for Surgery in Ischaemic / Functional MR

<table>
<thead>
<tr>
<th>Chronic Ischaemic MR</th>
<th>Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with severe MR, LV EF &gt; 30% undergoing CABG</td>
<td>IC</td>
</tr>
<tr>
<td>Patients with moderate MR undergoing CABG if repair is feasible</td>
<td>IIaC</td>
</tr>
<tr>
<td>Symptomatic patients with severe MR, LV EF &lt; 30% and option for revascularization</td>
<td>IIaC</td>
</tr>
<tr>
<td>Patients with severe MR, LVEF &gt; 30%, no option for revascularization, refractory to medical therapy, and low comorbidity</td>
<td>IIbC</td>
</tr>
</tbody>
</table>

**Functional MR:** surgery can be considered only in selected patients with severe symptoms despite optimal medical therapy.
Percutaneous Mitral Valve Repair
Prosthetic Ring Annuloplasty
Percutaneous Mitral Valve Repair
Prosthetic Ring Annuloplasty

Mitral valve

Coronary sinus

Tricuspid valve
Percutaneous Mitral Annuloplasty
The Monarc Device (Edwards Lifesciences)

8.8F Delivery system
Small anchor (Great cardiac vein)
Large anchor (CS ostium)

12F Guide catheter and dilator
Foreshortening Bridge
Percutaneous Mitral Annuloplasty
The Carillon Device (Cardiac Dimensions Inc.)
Percutaneous Mitral Annuloplasty
The PTMA Implant System (Viacor Inc)
# Percutaneous Mitral Annuloplasty

## Feasibility / Safety at 30 Day

<table>
<thead>
<tr>
<th></th>
<th>Monarc*</th>
<th>Carillon †</th>
<th>Viacor ‡</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>n=</strong></td>
<td>72</td>
<td>48</td>
<td>27</td>
</tr>
<tr>
<td>Success implantation (%)</td>
<td>82</td>
<td>63</td>
<td>48</td>
</tr>
<tr>
<td>In-hospital death (%)</td>
<td>0</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Myocardial infarction (%)</td>
<td>4</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Tamponade (%)</td>
<td>3</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Dissection of coron. sinus (%)</td>
<td>0</td>
<td>6</td>
<td>NA</td>
</tr>
</tbody>
</table>

* TCT 2008
† Circulation 2009;120:326-33
‡ Circ Cardiovasc Intervention 2009;2:277-84
# Percutaneous Mitral Annuloplasty

## Efficacy

<table>
<thead>
<tr>
<th></th>
<th>Monarc*</th>
<th>Carillon†</th>
<th>Viacor‡</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=27</td>
<td>n=23</td>
<td>n=9</td>
</tr>
<tr>
<td>Pre</td>
<td>1 yr</td>
<td>Pre</td>
<td>6 Mo.</td>
</tr>
<tr>
<td>Reduction MR ≥1/4 (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>-</td>
<td>59</td>
<td>-</td>
</tr>
<tr>
<td>ERO (cm²)</td>
<td>0.22</td>
<td>0.16</td>
<td>0.25</td>
</tr>
<tr>
<td>Rvol (ml)</td>
<td>32</td>
<td>25</td>
<td>35</td>
</tr>
</tbody>
</table>

* TCT 2008
† Circulation 2009;120:326-33
‡ Circ Cardiovasc Intervention 2009;2:277-84
Coronary Compression

• Monarc

  50 Patients
  Baseline & 90-Day Angio

  35 Patients
  No Coronary Vessel Changes

  15 Patients (30%)
  Coronary Vessel Changes
  (3MI’s (1death))

  9 Patients
  Bridge Compression

  5 Patients
  Anchor Compression

  1 Patient
  Anchor & Bridge Compression

  5 Faulty devices
  4 Device separation
  1 Device slippage

• Carillon

  6 cases (12%) of coronary compression (device recaptured)
  (Schofer et al. Circulation 2009;120:326-33)
CT Imaging
Percutaneous Mitral Valve Repair
Edge-to-Edge Technique in Ischaemic/Functional MR

**EVEREST: Event Free Clinical Success**

Patients with Acute Procedural Success (n = 79)

<table>
<thead>
<tr>
<th>Time (months)</th>
<th>Probability of Event Free Clinical Success</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>100%</td>
</tr>
<tr>
<td>6</td>
<td>99%</td>
</tr>
<tr>
<td>12</td>
<td>97%</td>
</tr>
<tr>
<td>18</td>
<td>97%</td>
</tr>
<tr>
<td>24</td>
<td>97%</td>
</tr>
<tr>
<td>30</td>
<td>97%</td>
</tr>
<tr>
<td>36</td>
<td>100%</td>
</tr>
<tr>
<td>42</td>
<td>90%</td>
</tr>
</tbody>
</table>

- **Freedom From Death**: 85%, 72%, 68%, 68%, 68%, 67%, 67%
- **Freedom From Surgery**: 100%, 99%, 97%, 97%, 97%, 97%, 97%
- **Freedom From Death, Surgery or MR >2+**: 68, 61, 42, 36, 28

*(Feldman. TCT 10/07)*
Conclusion (I)

• TAVI is a major change in the management of AS
  – Acquired experience
  – Number of potential candidates

• Present and future challenges
  – Technical improvements
  – Improved safety (imaging, experience…)
  – Thorough evaluation of results

• Patient selection will be a major issue
  – Be careful in extending use in patients at lower risk
  – Not to go too far in high-risk patients
  – Importance of a team approach and clinical judgment
Conclusion (II)

- The first steps of percutaneous mitral repair have been made in functional / ischaemic MR
- Pending questions remain on safety and efficacy
- Results should be carefully evaluated in comparison to surgery and contemporary medical treatment
Percutaneous valve interventions

- Are appealing given epidemiologic changes
- Expand the scope of interventions in high-risk patients
- Require a multidisciplinary approach at all steps
- Should be evaluated in the light of other approaches (need for large registries and randomised trials)