Valvular Heart Disease in Europe: Reality and Challenges

Carlos Aguiar, FESC
Sun City, October 27, 2015

I have no conflicts of interest with respect to the contents of this presentation
Valvular Heart Disease in Europe

Reality

- Epidemiology of VHD
- Evidence base of VHD management
- Gaps between evidence and practice

Challenges

- Changes in patient characteristics
- Changes in and emerging etiologies
- Bridging the gaps in VHD
VHD is Common

Overall age-adjusted prevalence of VHD is estimated at 2.5% and increases substantially after the age of 65 years

Prevalence of moderate/severe aortic and mitral valve diseases according to age (population-based US series of 11,911 Pts)

- Aortic stenosis: 0.4%
- Aortic regurgitation: 0.5%
- Mitral stenosis: 0.1%
- Mitral regurgitation: 1.7%

Gender does not affect prevalence
VHD is More Often Degenerative

Most common etiology is degenerative (63%) followed by rheumatic (22%)

Euro Heart Survey: 5,001 Pts from 92 centers in 25 European countries

Native VHD: 3,532 Pts (72%)
- Aortic stenosis 33.9%
- Aortic regurgitation 10.4%
- Mitral stenosis 9.5%
- Mitral regurgitation 24.8%
- Isolated right VHD 1.2%
- Multiple VHD 20.2%

Prior VHD surgery 1,469 Pts

Iung B et al. Eur Heart J 2003;24:1231
**VHD is More Often Degenerative**

Aortic stenosis, mitral regurgitation and multiple VHD are common in the elderly

**Euro Heart Survey:**
5,001 Pts from 92 centers in 25 European countries

<table>
<thead>
<tr>
<th></th>
<th>AS</th>
<th>AR</th>
<th>MS</th>
<th>MR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>69±12</td>
<td>58±16</td>
<td>58±13</td>
<td>65±14</td>
</tr>
<tr>
<td>Age &gt;70 (%)</td>
<td>56</td>
<td>25</td>
<td>18</td>
<td>44</td>
</tr>
<tr>
<td>Male (%)</td>
<td>57</td>
<td>74</td>
<td>19</td>
<td>52</td>
</tr>
</tbody>
</table>
VHD in Europe: Evidence Base

Reliable epidemiological data

- Diagnosis cannot rely only on clinical data
  - late onset of symptoms, cardiac murmurs lack specificity, surgical registries exclude nonsevere VHD and Pts denying/denied surgery
- Systematic echocardiography in a representative population allows unbiased determination of VHD prevalence, but is not practical

Guidance on VHD management

- Few clinical trials
- Very few randomized clinical trials
No recommendation based on multiple randomized clinical trials or meta-analyses in ESC Guidelines

Excludes IE and Pregnancy sections
Guideline-Practice Gap in VHD

One of every 3-4 Patients with severe asymptomatic single-VHD is not treated according to recommendations

Euro Heart Survey: 1,269 Pts underwent intervention

NYHA class I patients:
- Aortic stenosis: 81/512
- Aortic regurgitation: 25/119
- Mitral stenosis: 6/112
- Mitral regurgitation: 23/155

Graph:
- Over-use of intervention
- Agreement
- Under-use of intervention

Iung B et al. Eur Heart J 2003;24:1231
### Guideline-Practice Gap in VHD

**31.8% Patients with severe symptomatic single-VHD did not undergo intervention**

#### Reasons for no intervention:
- **Non-cardiac**
  - Old age 27.6%
  - COPD 13.6%
  - Renal failure 6.1%
  - Life expectancy 19.3%
  - Life expectancy sole reason 1.3%

- **Cardiac**
  - Regression of symptoms under medical Rx 39.9%
  - End-stage disease 18.4%
  - Symptoms 2° CAD 14.9%
  - Recent MI 7.9%
  - Life expectancy sole reason 1.3%

**Euro Heart Survey:**
- 1,817 Pts with severe symptomatic single-VHD

**Type of VHD:**
- Aortic stenosis \( n=809 \)
- Aortic regurgitation \( n=546 \)
- Mitral stenosis \( n=230 \)
- Mitral regurgitation \( n=232 \)

*Iung B et al. Eur Heart J 2003;24:1231*
Guideline-Practice Gap in VHD

Surgery is not performed in many patients with severe symptomatic aortic stenosis

Guideline-Practice Gap in VHD

Surgery is not performed in 33% patients ≥75 yrs old with severe symptomatic aortic stenosis

Euro Heart Survey: 216 Pts with severe isolated AS and angina / NYHA III-IV

- **Age** and **LVEF** are strong independent predictors of decision to not operate
- **Comorbidities** are common (44%) but only neurological dysfunction is independently associated with decision to not operate
- Only 7/72 patients (10%) refused surgery

www.escardio.org

Iung B et al. Eur Heart J 2005;26:2714
Guideline-Practice Gap in VHD

Surgery is not performed in 49% patients ≥75 yrs old with severe symptomatic mitral regurgitation

Euro Heart Survey: 396 Pts with isolated severe MR

- **Age** and LVEF are strong independent predictors of decision to not operate
- **Comorbidities** are common (40%) and also predict decision to not operate
- Non-ischemic MR and grade 3/4 MR associated with decision to not operate

Mirabel M et al. Eur Heart J 2007;28:1358

www.escardio.org
**Guideline-Practice Gap in VHD**

Old age in itself is not a valid reason to deny aortic valve replacement in severe aortic stenosis

- Octogenarians had an independently **risk of complications**: new renal failure (11.7% vs 4.2%), prolonged ventilation (12.4% vs 7.2%), GI complications (3.0% vs 1.3%) and longer mean ICU LOS (64 h vs 47 h)
- **Lower 5-yr survival post-AVR** in octogenarians (72% vs 89%) but comparable to that of age-matched Australian population

Isolated AVR in 2790 Pts included in a national database of the Australian Society of Cardiac and Thoracic Surgeons, between June 2001 and December 2009

Challenges in VHD

- Patients with severe symptomatic VHD have **reduced longevity and QoL** in the absence of successful valve repair or replacement procedures, and this also applies to selected asymptomatic patients with severe VHD.

- Appropriate selection of the **timing and type of valve procedure** is key to optimize the benefit-risk ratio of the intervention and patient outcomes.

- To correctly avoid **inappropriate treatment delays**, we need better knowledge of the **natural history of disease** and better **imaging and quantitation methods**.

- Better outcomes from **interventions** and less invasive interventions are needed to extend treatment to a growing **older and sicker population** of patients.
Challenges in VHD: More (Elderly) Pts

Population structure by 5-yr age groups and sex, EU-28

- **80+ Yrs**
  - **2013:** 5.1%
  - **2060:** 11.8%

**Life expectancy**
- **2013:** 77.6 yrs
- **2060:** 84.0 yrs

**2013**
- **Males:** 83.1 yrs
- **Females:** 89.1 yrs

**2060**
- **Males:** 84.0 yrs
- **Females:** 90.1 yrs

Challenges in VHD: More (Sicker) Pts

Comorbidities and associated cardiac diseases are common in aortic stenosis

Faggiano P et al. Int J Cardiol 2012;159:94
Challenges in VHD: More (Sicker) Pts

Comorbidities and associated cardiac diseases influence management and outcomes in aortic stenosis

- Increased **operative risk**
  (e.g. CKD, anemia)

- Poorer **long-term survival after intervention**
  (e.g. CKD, anemia, pulmonary hypertension)

- Which disease to blame for **symptoms**?
  (e.g. angina in the presence of CAD and AS)

- Which **management strategy** is best?
  (e.g. functional/ischemic MR may improve after isolated AVR, but not rheumatic/myxomatous)
Challenges in VHD: Reoperations

Cardiac reoperations are increasingly common due to improving long-term survival after cardiac surgical interventions

<table>
<thead>
<tr>
<th>Challenge</th>
<th>OR</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Injury</td>
<td>2.59</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Radiotherapy</td>
<td>3.37</td>
<td>0.001</td>
</tr>
<tr>
<td>Preop renal failure</td>
<td>1.89</td>
<td>0.003</td>
</tr>
<tr>
<td>Urg/emerg state</td>
<td>2.86</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Preop card shock</td>
<td>5.68</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>NYHA III-IV</td>
<td>3.25</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Prior CABG</td>
<td>1.92</td>
<td>0.001</td>
</tr>
<tr>
<td>Prior AV op</td>
<td>1.91</td>
<td>0.001</td>
</tr>
<tr>
<td>Current AV op</td>
<td>1.58</td>
<td>0.008</td>
</tr>
</tbody>
</table>

2555 Patients undergoing repeat median sternotomy for routine cardiac surgery, 2006-2007

Independent predictors of hospital mortality (7.3%)

- Challenges: greater technical complexity, risk of injury to cardiac structures and previously placed bypass grafts
- Several protective strategies: preoperative CT; peripheral cannulation for cardiopulmonary bypass, and institution of bypass before sternotomy
Challenges in VHD: Emerging Etiologies

Increasing number of cancer survivors, who may suffer from adverse cardiovascular effects of radiation therapy

**Radiation-induced VHD**: common finding in post-mortem studies (81%); more commonly involves AV and MV; diagnosis of asymptomatic RIVD occurs at mean 11.5 yrs after irradiation (vs 16.5 yrs for symptomatic Pt).

Doppler echocardiogram of the aortic valve (done in 2005) shows moderate aortic stenosis and aortic regurgitation in a 46-year-old female who had received radiation therapy for Hodgkin’s disease in 1976. Some degree of regurgitation was noted in all 4 valves.
Challenges in VHD: Emerging Etiologies

Few months of exposure to agonists of the 5-HT$_{2B}$ receptor, highly present in valve tissue, may induce VHD

- Common histology in **drug-induced VHD**: tissue thickening, abundant extracellular matrix of glycosaminoglycans and collagen, proliferation of myofibroblasts and smooth muscle cells, few calcifications, no pronounced inflammation (restricted valve motion -> regurgitation)

Challenges in VHD: Decision-Making

Factors affecting decision-making in severe aortic stenosis

- **Comorbidities** and associated cardiac diseases (frailty, pre-operative evaluation)

- “Overestimation” of **operative risk** (logistic Euroscore, Ambler score)

- “Underestimation” of **symptoms** (age, poor mobility, concomitant diseases)

- “Underestimation” of **hemodynamic severity** (low-flow/low-gradient)
Transcatheter Valve Implantation addresses an unmet need in severe symptomatic aortic stenosis


Reasons for “inoperable”:
- Porcelain aorta (15.1%)
- Chest-wall deformity or deleterious effects of chest-wall irradiation (13.1%)
- \(O_2\)-dependent respiratory insufficiency (23.5%)
- Frailty (23.1%)

HR 0.55 (P<0.001)

NNT = 5

Bridging the Gap in VHD: TMVR

Transcatheter mitral valve therapies have emerged as an alternative in high surgical risk or inoperable patients.

- MitraClip (Abbot Vascular)
  Edge-to-edge repair

- NeoChord (NeoChord DS1000)
  Chordal repair

- CARILLON (Cardiac Dimensions)
  Indirect Annuloplasty

- Mitralign Bident (Mitralign)
  Direct annuloplasty

- Cardioband TF (Valtech)
  Direct annuloplasty

- TMVI-TA (CardiAQ)
  TMVI-TF (CardiAQ)

Maisano F et al. Eur Heart J 2015;36:1651
Bridging the Gap in VHD: Valve Clinics

Rationale: \( \uparrow \) patients, changing characteristics, \( \uparrow \) technologies for refined diagnosis and treatment, dismal prognosis if overlooked.

Objectives:
- Improve patient care
- Optimize use of proven diagnostic tests and therapies
- Improve adherence to current evidence and guidelines
- Patient education
- Improve quality of life
- Reduce VHD-related healthcare costs
Valvular Heart Disease in Europe

- VHD is common, and degenerative aortic stenosis and mitral regurgitation are the most common forms in Europe.
- Changes in patient characteristics (older age, comorbidities, associated cardiac diseases and emerging etiologies) have increased surgical risk and the complexity of decision-making.
- Older patients and those with depressed LV systolic function are often not treated, illustrating a knowledge gap in the management of VHD.
- Better outcomes from interventions, less invasive interventions, and organization of patient care (heart valve clinics) may ultimately reduce the burden of VHD in Europe.