The Management of Aortic Stenosis

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Auckland Heart Group
Mid Winter Symposium 2011
Mrs T

- 60 year old woman
- Usually fit and well, perhaps slowing down a bit over last year
- Walked the Inca trail in 2009
- Recently very short of breath and tight in chest when walking her dog
- Loud systolic heart murmur noted - not noted before
Examination

- Sinus rhythm, BP 136/70
- Slow rising pulse
- Grade $\frac{3}{4}$ late peaking ejection systolic murmur at base preceded by an ejection click, radiating to both carotids
- Single S2
- No diastolic murmur
- Soft pan systolic murmur at apex
- No radiofemoral delay
What do patients ask?

• Is there anything I can do to stop the problem progressing
• What sort of exercise should I do/not do?
• When should I have my operation?
• Why don’t you just replace the valve now?
• What are the risks of an operation?
• How long will my new valve last?
• Am I feeling tired/ breathless/ dizzy because of my valve problem?
• Will I still need to take all these pills after the operation?
Natural History of Aortic Stenosis

Ross J, Jr, Braunwald E. Circulation 1968
Aortic Stenosis

• AS is a consistently progressive disease that affects 2-7% of individuals older than age 65

• Natural history of symptomatic aortic stenosis (AS) is poor.

• Medically treated patients have a 1 and 5 year survival of 60% and 32%

• Aortic valve replacement is the most common heart valve procedure
Wide individual variability in hemodynamic progression- average 0.3 m/s/yr, AVA 0.1 cm²/yr

74% had undergone AVR by 5 years

Primary indication for AVR was decreased exercise tolerance in 38%, heart failure in 23%, angina in 15%, syncope/presyncope in 12%

Baseline Vmax, functional status score, and rate of change of aortic velocity were only multivariate predictors of outcome
Event free survival in asymptomatic aortic stenosis

Event free survival in asymptomatic AS

Aortic Stenosis-Assessment

- Definition of aetiology of stenosis
- Quantitation of stenosis severity
- Evaluation of coexisting valvular lesions
- Response of cardiac chambers to chronic pressure overload
Calcific

DIASTOLE
Thick, stiff leaflets
No commissural fusion

SYSTOLE

Bicuspid
Bicuspid with raphe
Secondary calcification

Rheumatic
Commissural fusion.
Mitral valve affected

Calcific aortic stenosis

- Most common acquired valve lesion
- Usually presents 70-85 years old
- Active disease process with lipid accumulation, inflammation, and calcification
- 2D imaging - echogenicity and thickening, reduced opening of leaflets
Critical calcific aortic stenosis
Afterload mismatch
Bicuspid aortic valve
Differential diagnosis

• Valvular aortic stenosis
  – Calcific AS
  – Bicuspid valve with calcification
  – Rheumatic AS
  – Congenital As (unicuspid valve)

• Subaortic stenosis
  – membranous
  – Muscular
  – Dynamic

• Supravalvular AS
VALVULAR AORTIC STENOSIS

SUBAORTIC MEMBRANE

HYPERTROPHIC CARDIOMYOPATHY

From: Otto CM.
Textbook of Clinical Echocardiography 1st ed
Quatitation of stenosis severity

- **Simplified Bernoulli equation**
  \[ \Delta P_{\text{max}} = 4 \times V_{\text{max}}^2 \]
  \[ \Delta P_{\text{mean}} = \frac{\Delta P_{\text{max}}}{1.45 + 2 \text{ mmHg}} \]
  or \[ \Delta P_{\text{mean}} = 2.4 \times (V_{\text{max}})^2 \]

- **Pressure gradients dependent on flow rate**

- **Continuity equation**
  \[ \text{AVA} = \text{CSA}_{LVOT} \times \frac{\text{VTI}_{LVOT}}{\text{VTI}_{Ao}} \]
The Continuity Equation

\[ Q_1 = Q_2 \]

\[ Q_1 = A_1 \times V_1 = A_2 \times V_2 \]

\[ A_2 = \frac{Q_1}{V_2} \]
## Grading Aortic Stenosis Severity

<table>
<thead>
<tr>
<th></th>
<th>$V_{\text{max}}$ (m/s)</th>
<th>$P_{\text{max}}$(mmH)</th>
<th>$P_{\text{mean}}$ (mmHg)</th>
<th>AVA</th>
<th>AVA Indexed (cm$^2$/m$^2$)</th>
<th>Velocity ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Normal</strong></td>
<td>&lt;2.5</td>
<td>&lt;16</td>
<td>25</td>
<td>&gt;2.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Mild</strong></td>
<td>2.6-2.9</td>
<td>&lt;36</td>
<td>&lt;20 (&lt;30&lt;sup&gt;a&lt;/sup&gt;)</td>
<td>&gt;1.5</td>
<td>&gt;0.85</td>
<td>&gt;0.5</td>
</tr>
<tr>
<td><strong>Moderate</strong></td>
<td>3.0-4.0</td>
<td>36-64</td>
<td>20-40&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1.0-1.5</td>
<td>0.60-0.85</td>
<td>0.25-0.5</td>
</tr>
<tr>
<td><strong>Severe</strong></td>
<td>&gt;4.0</td>
<td>&gt;64</td>
<td>&gt;40&lt;sup&gt;b&lt;/sup&gt; &gt;50&lt;sup&gt;a&lt;/sup&gt;)</td>
<td>&lt;1.0</td>
<td>&lt;0.6</td>
<td>&lt;0.25</td>
</tr>
</tbody>
</table>

<sup>a</sup> ESC Guidelines  <sup>b</sup> AHA/ACC Guidelines
How often should I have a follow up and/or an echo?

• Depends on AS severity and other conditions
• Annual medical examination for asymptomatic AS of any degree
• Discussion about development and reporting of any symptoms
• Echo frequency-
  – Mild AS every 3-5 years
  – Moderate AS every 1-2 years
  – Severe AS- every year
  – If change in symptoms
Is there anything I can do/take to cure the problem?

- Treat coexistent hypertension and hyperlipidaemia
- 4 randomised controlled trials of statin therapy in asymptomatic AS – no evidence of any slowing of AS progression
- ACE inhibitors, aldosterone antagonist- no effect on progression
- Physical activity
  - no restriction in mild AS
  - Avoid competitive sports in moderate to severe AS
- Concurrent illness
  - Dehydration, anaemia, thyroid disease, other cardiac disease
Promptly report symptoms!

- Exercise intolerance
- Fatigue
- Exertional breathlessness
- Presyncope or syncope
- Exertional chest pain /discomfort /tightness
Why do we monitor patients with valvular heart disease? When is the “golden moment”

• Not too early and not too late!

• Avoid complications of native valve disease
  – Death, heart failure (systolic and diastolic), arrhythmias, thromboembolism, exercise intolerance

• Avoid complications of prosthetic valve disease
  – Death, infection, bleeding, thromboembolism, valve deterioration, patient valve mismatch, hemolysis

• Timing is everything
How do we monitor patients with valvular heart disease?

- Listen to the patient, look at the valve
- Clinical examination
- Transthoracic echocardiography
- Transesophageal echocardiography
- Exercise testing
- Dobutamine and exercise stress stress echo
- MRI
- CT
- Cardiac catheterization
ACC/AHA GUIDELINES FOR AVR IN AS

- Symptomatic patients with severe AS I
- Severe AS undergoing CABG I
- Severe AS and aortic or valve surgery I
- Moderate AS and CABG, aortic or valve SX IIa
- Asymptomatic severe AS and
  - LV systolic dysfunction IIa
  - Abnormal response to exercise (eg hypotension) IIa
  - Ventricular tachycardia IIb
  - Marked or excessive LVH (>15 mm) IIb
  - Valve area <0.6 cm² IIb

- Prevention of SCD in asymptomatic patients with none of the above III
How do you know the symptoms are due to the valve?
Why not just ask the patient?

- Reduced exercise tolerance is the most common symptom—difficult in the elderly, may avoid or be unable to exercise
- Patients may not report or recognise symptoms—“just getting older”
- Symptoms of dizziness, “turns”, breathlessness often multifactorial
Problems with a “wait for symptoms” strategy

- Patients do not immediately report new symptoms
- Patients who become symptomatic are at risk while waiting for surgery
- Operative risk increases with symptom severity
Why operate before symptoms occur?

- Very severe disease
- Rapidly progressive stenosis
- Evidence of left ventricular systolic dysfunction
- Patients who live in remote areas
- Long surgical waiting lists
- Patients who do heavy physical exertion
- Patients who plan pregnancy
- Those with significant LV hypertrophy and diastolic dysfunction
Why not operate before symptoms occur?

Complication rate of AVR

- Risk of sudden death <1% per year in truly asymptomatic individuals
- Operative mortality approximately 2-9%, AVR plus CABG 4-24%
- Prosthetic valve complications 2-3 % per patient year
  - thromboembolism
  - patient - valve mismatch
  - structural valve deterioration
  - endocarditis
  - hemolysis
Increased Plasma Natriuretic Peptide Levels Reflect Symptom Onset in Aortic Stenosis

Ivor L. Gerber, MB, ChB; Ralph A.H. Stewart, MD; Malcolm E. Legget, MB, ChB; Teena M. West, MSc; Renelle L. French; Timothy M. Sutton, MB, ChB; Timothy G. Yandle, PhD; John K. French, MB, PhD; A. Mark Richards, MD, DSc; Harvey D. White, MB, DSc
Median N-BNP by Severity of Aortic Stenosis

- Controls (N=100)
- AVA $\geq$ 1.0 (N=15)
- AVA < 1.0 (N=16)
- AVA < 1.0 EF $\geq$ 50% (N=35)
- AVA < 1.0 EF < 50% (N=8)

P < 0.0001
The figure illustrates the levels of N-BNP (pmol/l) by NYHA Class in Aortic Stenosis. The graph shows a significant increase in N-BNP levels with higher NYHA Classes. Controls (n=100) have the lowest levels, followed by Class I (n=29), Class II (n=29), and Class III/IV (n=16) with the highest levels. The difference is statistically significant (P < 0.0001).

N-BNP and Aortic Valve Area

N-BNP (pmol/l)

Aortic Valve Area (cm²)

Symptomatic
Asymptomatic

60*

0

0 0.5 1.0 1.5 2.0
N-BNP and symptoms in aortic stenosis

Exercise Testing in Asymptomatic Aortic Stenosis

- Only safe in truly asymptomatic patients
- Lack of rise or fall in BP indicative of poor prognosis
- Doppler measures of latent left ventricular dysfunction promising
Control Patient

Rest

Post exercise

HR 70/min

HR 106/min

Aortic Stenosis Patient

Rest

Post exercise

Patients with aortic stenosis stratified according to percentage change of peak S’ velocity after exercise.

Patients with a <30% increase in peak S’ velocity (black) after exercise were significantly worse clinically than those with a >30% increase in peak S’ velocity (red) ($p=0.04$, log-ranked test).

Not all are suitable for AVR

• Operative mortality in large series for AVR 4% (n= 32,968)
• Age, LV dysfunction, renal impairment, COPD etc substantially increase risk
• Euro Heart Survey – 32% of patients with severe symptomatic valvular heart disease did not undergo surgery because of co-morbidities

Edwards FH et al. JACC 2001;37:885-92
Iung B et al. Eur Heart J 2003;24:1231-1243
Percutaneous Transcatheter Implantation of an Aortic Valve Prosthesis for Calcific Aortic Stenosis
First Human Case Description
Alain Cribier, MD et al. (*Circulation*. 2002;106:3006-3008.)
Transcatheter Aortic-Valve Implantation for Aortic Stenosis in Patients Who Cannot Undergo Surgery

Martin B. Leon, M.D., Craig R. Smith, M.D., Michael Mack, M.D., D. Craig Miller, M.D., Jeffrey W. Moses, M.D., Lars G. Svensson, M.D., Ph.D., E. Murat Tuzcu, M.D., John G. Webb, M.D., Gregory P. Fontana, M.D., Raj R. Makkar, M.D., David L. Brown, M.D., Peter C. Block, M.D., Robert A. Guyton, M.D., Augusto D. Pichard, M.D., Joseph E. Bavaria, M.D., Howard C. Herrmann, M.D., Pamela C. Douglas, M.D., John L. Petersen, M.D., Jodi J. Akin, M.S., William N. Anderson, Ph.D., Duolao Wang, Ph.D., and Stuart Pocock, Ph.D., for the PARTNER Trial Investigators*
PARTNER Study Design

Symptomatic Severe Aortic Stenosis

ASSESSMENT: High Risk AVR Candidate
3105 Total Patients Screened

Total = 1058 patients

2 Parallel Trials: Individually Powered

n= 700
High Risk

High Risk TF

1:1 Randomization

TAVI Trans femoral

Primary Endpoint: All Cause Mortality (1 yr) (Non-inferiority)

Inoperable

n=358

High Risk TA

1:1 Randomization

TAVI Trans apical

Primary Endpoint: All Cause Mortality over length of trial (Superiority)

ASSESSMENT: Transfemoral Access

1:1 Randomization

Surgical AVR

1:1 Randomization

Surgical AVR

ASSESSMENT: Transfemoral Access

1:1 Randomization

Standard Therapy (usually BAV)

Not In Study
1 yr Endpt - All Cause Mortality

\[ \Delta \text{ at 1 yr} = 20.0\% \]
\[ \text{NNT} = 5.0 \text{ pts} \]

Numbers at Risk

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<thead>
<tr>
<th></th>
<th>TAVI</th>
<th>Standard Rx</th>
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<tbody>
<tr>
<td>1yr</td>
<td>179</td>
<td>179</td>
</tr>
<tr>
<td>6</td>
<td>138</td>
<td>121</td>
</tr>
<tr>
<td>12</td>
<td>122</td>
<td>83</td>
</tr>
<tr>
<td>18</td>
<td>67</td>
<td>41</td>
</tr>
<tr>
<td>24</td>
<td>26</td>
<td>12</td>
</tr>
</tbody>
</table>
**Cardiovascular Mortality**

- **Standard Rx**
- **TAVI**

- **Numbers at Risk**
  - **TAVI:** 179, 138, 122, 67, 26
  - **Standard Rx:** 179, 121, 83, 41, 12

- **Δ at 1 yr = 24.1%**
- **NNT = 4.1 pts**

- **Cardiovascular mortality (%)**

  - TAVI: 44.6%
  - Standard Rx: 20.5%
Transcatheter versus Surgical Aortic-Valve Replacement in High-Risk Patients

Craig R. Smith, M.D., Martin B. Leon, M.D., Michael J. Mack, M.D., D. Craig Miller, M.D., Jeffrey W. Moses, M.D., Lars G. Svensson, M.D., Ph.D., E. Murat Tuzcu, M.D., John G. Webb, M.D., Gregory P. Fontana, M.D., Raj R. Makkar, M.D., Mathew Williams, M.D., Todd Dewey, M.D., Samir Kapadia, M.D., Vasilis Babaliaros, M.D., Vinod H. Thourani, M.D., Paul Corso, M.D., Augusto D. Pichard, M.D., Joseph E. Bavaria, M.D., Howard C. Herrmann, M.D., Jodi J. Akin, M.S., William N. Anderson, Ph.D., Duolao Wang, Ph.D., and Stuart J. Pocock, Ph.D., for the PARTNER Trial Investigators*
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<thead>
<tr>
<th></th>
<th>Partner A TAVI</th>
<th>Partner A SAVR</th>
</tr>
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<tbody>
<tr>
<td><strong>M and M</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Euroscore (%)</strong></td>
<td>29.3</td>
<td>29.2</td>
</tr>
<tr>
<td><strong>30 day</strong></td>
<td>3.4%</td>
<td>6.5%</td>
</tr>
<tr>
<td><strong>1 year</strong></td>
<td>24.2%</td>
<td>26.8%</td>
</tr>
<tr>
<td><strong>1 year cardiac</strong></td>
<td>14%</td>
<td>13%</td>
</tr>
<tr>
<td><strong>Stroke/TIA 30 day (major stroke)</strong></td>
<td>5.5% (3.8)</td>
<td>2.4%* (2.1)</td>
</tr>
<tr>
<td><strong>Stroke/TIA 1 year (major stroke)</strong></td>
<td>8.3% (5.1)</td>
<td>4.3% * (2.4)</td>
</tr>
<tr>
<td><strong>Major bleeding</strong></td>
<td>9.3%</td>
<td>19.5%*</td>
</tr>
<tr>
<td><strong>New onset AF</strong></td>
<td>8.6%</td>
<td>16.0%*</td>
</tr>
<tr>
<td><strong>Vascular comp</strong></td>
<td>17%</td>
<td>3.8%*</td>
</tr>
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Edwards Sapien Transcatheter Aortic Valve

- Stainless steel frame
- Bovine pericardium
- Balloon Expandable

On delivery system

Deployed by balloon expansion
Deployment of an Edwards Sapien valve

Balloon valvuloplasty

Crossing the native valve

Balloon expansion deploys the Edwards valve during rapid pacing
CoreValve

Nitinol self expanding frame

Leaflets made from porcine pericardium

18F (6mm) delivery

Can be repositioned before final deployment

Percutaneous (unless cut down to eg subclavian)

Higher need for pacemaker

More AR than Edwards?
With the device across the diseased valve, the sheath is withdrawn (black arrow) so that the self-expanding frame is no longer constrained and can open up (white arrow)
Mercy Experience 2008-2011

- August 08- February 2011: 48 patients
  - CoreValve: 40
  - Edwards: 8
- Mean age: 85 years (44-96 yr)
- Symptomatic Class III/IV: 42/48
- Mean Logistic Euroscore: 20.9% (7.4-52.3)
Echo Characteristics

► Severe AS –
  peak aortic velocity 4.4 ± 1.5 m/s (3.1-5.5)
  peak gradient 80 ± 49 mmHg (23-132)
  mean gradient 51 ± 34 mmHg (31-85)

► AVA
  0.7 ± 0.7 cm² (0.4-1.3)

► LV EF
  51% (range 30-78%)

► LVEF <50%
  12/48 (25%)
Procedural Data

- General Anaesthesia: 48/48
- Percutaneous closure: 48/48
- Post-procedural gradient: trivial
- Post-procedural AR < grade 2: 43/48
- Procedure time, mins, mean (range): 79 (39-164)
- ICU: 23hr (0-72)
- Post-procedural days in hospital: 7.1 (3-22)
- No referral post procedure for cardiac surgery
Mortality

- Death during procedure  ____ 1
- Death within 30 days  ____ 1
Morbidity

- Transfusion: 27/48 (56%)
- Stroke/TIA: 1/48 (2%)
- Renal function deterioration: 4 (8%)
- Pacemaker post procedure: 12/48 (26%)
- Pacemaker n (%) CoreValve: 12/40 (30%)
- Pacemaker n (%) Edwards: 0/8 (0%)
- Conversion to cardiac surgery: Nil
- Peripheral vascular surgery/thrombin: 1/2
Late Follow Up

- **Late death**
  - Acute coronary syndrome 1
  - Cerebral haemorrhage 2
  - Cancer 1
  - Respiratory failure 2
  - Septicaemia 1
- **Moderate / severe AR** 2/2
- **Readmission** –
  - 19 patients, 43 admissions, 13 cardiac
- **Sustained symptomatic improvement at 1 year in 34/35 Corevalve patients still alive**
Ms O

► 76 yr old
► In 2000, she had surgical replacement of her calcified stenotic native aortic valve with a size 21 Carpentier Edwards bovine pericardial prosthesis
► Fragile aorta and pericardial patch to aortotomy site
► COPD FEV1/FVC 0.73/1.32
► 2008 progressively more breathless. NT-ProBNP 145mol/L (N <35)
► Serial echo increasing AS and AR – valve area 0.8 and mod AR
► EF fell from 53% to 38%
► Euroscore 31% and STS 40%
Ms O’C. CoreValve across failed Carpentier Edwards surgical valve

Flotation pacemaker from Jugular

Superstiff wire looped in LV
Not fully released
The gradient across the aortic valve is abolished.
CONCLUSIONS

• Aortic stenosis is a common condition
• Symptoms may be insidious, serial monitoring is important
• Echo is mainstay, with other tests providing supportive information
• Aortic valve replacement is the definitive treatment either by surgical or percutaneous routes
• Transcatheter approach will revolutionise the treatment of valve disease
“Listen to the patient, look at the valve”
Thank you!