“Low flow low gradient and What I Really Need to Know from the 2014 Guidelines for the Management of Patients with Valvular Heart Disease”
Pieter Kappetein,
Dept Cardio-thoracic Surgery
Erasmus University Medical Center
Rotterdam, The Netherlands
Martinus Theunis Steyn

6th State President of the Orange Free State

In office
4 March 1896 – 30 May 1902
Guidelines on the management of valvular heart disease (version 2012)

The Joint Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

Authors/Task Force Members: Alec Vahanian (Chairperson) (France), Ottavio Alfieri (Chairperson) (Italy), Felicita Andreotti (Italy), Manuel J. Antunes (Portugal), Gonzalo Barón-Esquivias (Spain), Helmut Baumgartner (Germany), Michael Andrew Borger (Germany), Thierry P. Carrel (Switzerland), Michele De Bonis (Italy), Arturo Evangelista (Spain), Volkmar Falk (Switzerland), Bernard Jung (France), Patrizio Lancellotti (Belgium), Luc Pierard (Belgium), Susanna Price (UK), Hans-Joachim Schäfers (Germany), Gerhard Schuler (Germany), Janina Stepinska (Poland), Karl Swedberg (Sweden), Johanna Takkenberg (The Netherlands), Ulrich Otto Von Oppell (UK), Stephan Windecker (Switzerland), Jose Luis Zamorano (Spain), Marian Zembala (Poland)

ESC Committee for Practice Guidelines (CPG): Jeroen J. Bax (Chairperson) (The Netherlands), Helmut Baumgartner (Germany), Claudio Ceconi (Italy), Veronica Dean (France), Christi Deaton (UK), Robert Fagard (Belgium), Christian Funck-Brentano (France), David Hasdai (Israel), Arno Hoes (The Netherlands), Paulus Kirchhof (United Kingdom), Juhani Knuuti (Finland), Philippe Kolh (Belgium), Theresa McDonagh (UK), Cyril Moulin (France), Bogdan A. Popescu (Romania), Željko Reiner (Croatia), Udo Sechtem (Germany), Per Anton Sirnes (Norway), Michal Tendera (Poland), Adam Torbicki (Poland), Alec Vahanian (France), Stephan Windecker (Switzerland)

Document Reviewers: Bogdan A. Popescu (ESC CPG Review Coordinator) (Romania), Ludwig Von Segesser (EACTS) Review Coordinator (Switzerland), Luigi P. Badano (Italy), Matjaž Bunc (Slovenia), Marc J. Claesys (Belgium), Niksa Drinkovic (Croatia), Gerasimos Filippatos (Greece), Gilbert Habib (France), A. Pieter Kappetein (The Netherlands), Roland Kassab (Lebanon), Gregory Y.H. Lip (UK), Neil Moat (UK), Georg Nickenig (Germany), Catherine M. Otto (USA), John Pepper, (UK), Nicolo Piazza (Germany), Petronella G. Pieper (The Netherlands), Raphael Rosenhek (Austria), Naltin Shuka (Albania), Ehud Schwammenthal (Israel), Juerg, Schwitter (Switzerland), Pilar Tornos Mas (Spain), Pedro T. Trindade (Switzerland), Thomas Walther (Germany).
What Causes Aortic Stenosis in Adults?

More Common

- **Age-Related Calcific Aortic Stenosis**: Aortic stenosis in patients over the age of 65 is usually caused by calcific (calcium) deposits associated with aging.

- **Rheumatic Fever**: Adults who have had rheumatic fever may also be at risk for aortic stenosis.

Less Common

- **Congenital Abnormality**: In some cases adults may develop aortic stenosis resulting from a congenital abnormality.
Independent Risk Factors associated with degenerative aortic valve disease

- Increasing age
- Male gender
- Hypertension
- Smoking
- Elevated lipoprotein A
- Elevated LDL cholesterol
Sobering Perspective

5-Year Survival

Survival, %

- Breast Cancer: 23%
- Lung Cancer: 4%
- Colorectal Cancer: 12%
- Prostate Cancer: 30%
- Ovarian Cancer: 28%
- Severe Inoperable AS*: 3%

*Using constant hazard ratio. Data on file, Edwards Lifesciences LLC. Analysis courtesy of Murat Tuczu, MD, Cleveland Clinic

5 year survival of breast cancer, lung cancer, prostate cancer, ovarian cancer and severe inoperable aortic stenosis
## Indications for AVR in symptomatic AoS

<table>
<thead>
<tr>
<th>Indication</th>
<th>Class</th>
<th>Evidence Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe AS and any symptom related to AS</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Severe AS undergoing CABG, surgery Asc Ao, any other valve</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Should be considered in symptomatic patients with low flow, low gradient (&lt;40 mmHg) AS with normal EF only after careful confirmation of severe AS</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>Should be considered in high risk patients with severe symptomatic AS who are suitable for TAVI, but in whom surgery is favoured by a ‘heart team’ based on the individual risk profile and anatomic suitability</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>Should be considered in asymptomatic patients with severe AS and abnormal exercise test showing fall in blood pressure below baseline.</td>
<td>IIa</td>
<td>C</td>
</tr>
</tbody>
</table>
Patient Assessment
1. Is valvular heart disease severe?
Multiple Modalities May Be Used to Diagnose Severe Aortic Stenosis

- Auscultation
- Trans-thoracic Echo (TTE)
- Chest X-ray
- Cardiac Cath.
- Electrocardiogram
Schematic diagram of continuity equation

\[ A_2 = \frac{A_1 \cdot v_1}{v_2} \]
Echocardiographic criteria for the definition of Severe Aortic Valve stenosis

<table>
<thead>
<tr>
<th>Valve area (cm²)</th>
<th>&lt; 1.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indexed valve area (cm²/m² BSA)</td>
<td>&lt; 0.6</td>
</tr>
<tr>
<td>Mean gradient (mmHg)</td>
<td>&gt; 40</td>
</tr>
<tr>
<td>Maximum jet velocity (m/s)</td>
<td>&gt; 4.0</td>
</tr>
<tr>
<td>Velocity ratio</td>
<td>&lt; 0.25</td>
</tr>
</tbody>
</table>

Low Flow, Low Gradient AS

- Low gradient with a small calculated valve area in the setting of poor systolic function. This may result in lack of referral for AVR because of the low gradient.

- Dobutamine Stress Echo:
  - By increasing cardiac output, we can determine if the AS is severe by reassessing the gradient across the aortic valve (increases) AND the aortic valve area (decreases).
  - Assess myocardial contractile reserve
    - Does the cardiac output improve by 20% or more.
  - Critical for decision making regarding aortic valve replacement.
Low flow low gradient severe aortic stenosis
AVA < 1.0 cm²
LV Stroke index < 35 ml / m²
Mean gradient < 40 mmHg

LVEF

<50%
Classical Low flow Low gradient AS
Low dose dobutamine ECHO
AVA > 1.0 cm²
Mean gradient < 40 mmHg
Pseudo severe AS
AVA < 1.0 cm²
Mean gradient > 40 mmHg
True severe AS

>50%
Paradoxical Low flow Low gradient AS
Exclude error in measurement
Indexed AVA
No flow reserve
Increase stroke volume < 20%
AVA unchanged
Mean gradient unchanged
• Is valvular heart disease severe?

This big-stomach man is also carrying the risk of:
- Type II diabetes
- High blood pressure
- Elevated cholesterol
- Arthritis
- Depression
- Cardiac disease

You DON’T want to be him

ACT NOW!!

www.MexicoHealth.Com
Mortality Elderly Patients

1. Cognitive impairment: 5 - 25%
2. Functional impairment: 8 - 25%
3. Malnutrition: 5 - 13%
4. Frailty: 17 – 22%

1. Is valvular heart disease severe?
2. Does the patient have symptoms?
3. Are symptoms related to valvular disease?
4. What is life expectancy and expected QOL?
Life expectancy in elderly patients

Average Dutch Male

AVR + CABG

Bioprosthesis

Life Expectancy (years)

Age
1. Is valvular heart disease severe?
2. Does the patient have symptoms?
3. Are symptoms related to valvular disease?
4. What is life expectancy and expected QOL?
5. What is the risk / benefit ratio?
Risk scoring systems

Operative mortality risk (%)

Low risk:
75-year-old male
EF 55%
No comorbidities
Risk: 1.0-4.3%

High risk:
85-year-old female
EF 30%
Renal dysfunction
Pulmonary hypertension
Risk: 4.3-59.8%

“In the absence of a perfect quantitative score, the risk assessment should mostly rely on the clinical judgment of the ‘heart team’, in addition to the combination of scores.”
Risk scores

Comorbid Conditions
(not in scores)

Life expectancy

Risk estimation
Risk-Benefit ratio

Customized management decisions

Estimated QoL improvement
<table>
<thead>
<tr>
<th>Number</th>
<th>Question</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Is valvular heart disease severe?</td>
</tr>
<tr>
<td>2</td>
<td>Does the patient have symptoms?</td>
</tr>
<tr>
<td>3</td>
<td>Are symptoms related to valvular disease?</td>
</tr>
<tr>
<td>4</td>
<td>What is life expectancy and expected QOL?</td>
</tr>
<tr>
<td>5</td>
<td>What is the risk / benefit ratio?</td>
</tr>
<tr>
<td>6</td>
<td>What does the patient want?</td>
</tr>
</tbody>
</table>
1. Complex decisions

2. Great quantity of information

3. Susceptibility to framing effects increases with age

**Framing effect** is an example of cognitive bias, in which people react differently to a particular choice depending on whether it is presented as a loss or as a gain.
<table>
<thead>
<tr>
<th></th>
<th>Question</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Is valvular heart disease severe?</td>
</tr>
<tr>
<td>2</td>
<td>Does the patient have symptoms?</td>
</tr>
<tr>
<td>3</td>
<td>Are symptoms related to valvular disease?</td>
</tr>
<tr>
<td>4</td>
<td>What is life expectancy and expected QOL?</td>
</tr>
<tr>
<td>5</td>
<td>What is the risk / benefit ratio?</td>
</tr>
<tr>
<td>6</td>
<td>What does the patient want?</td>
</tr>
<tr>
<td>7</td>
<td>Local circumstances for treatment choice</td>
</tr>
</tbody>
</table>
For patients in whom TAVR or high-risk surgical AVR is being considered, members of a Heart Valve Team should collaborate to provide optimal patient care.

**Recommendation**

**Class** I

**Level** C

Vahanian & Alfieri et al. *Eur Heart J* 2012;33:2451-96
Nishimura RA et al. *Circulation* 129:e521-643
Valve + Coronary disease
Management of patients with coronary artery disease

Diagnosis of coronary artery disease

- Coronary angiography is recommended before valve surgery
- History of coronary artery disease
- Suspected myocardial ischemia
- Left ventricular dysfunction
- Men age > 40
- Postmenopausal women
- ≥1 cardiac risk factor

Class: I
Level: C
Indications for Transcathether Aortic valve implantation

<table>
<thead>
<tr>
<th>Indication</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAVI should only be undertaken with a multidisciplinary “heart team” including cardiologists and cardiac surgeons and other specialists if necessary.</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>TAVI should only be performed in hospitals with cardiac surgery on-site.</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>TAVI is indicated in patients with severe symptomatic AS who are not suitable for AVR as assessed by a “heart team” and who are likely to gain improvement in their quality of life and to have a life expectancy of more than 1 year after consideration of their comorbidities.</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>TAVI should be considered in high risk patients with severe symptomatic AS who may still be suitable for surgery, but in whom TAVI is favoured by a “heart team” based on the individual risk profile and anatomic suitability.</td>
<td>IIa</td>
<td>B</td>
</tr>
</tbody>
</table>

« At the present stage, TAVI should not be performed in patients at intermediate risk for surgery and trials are required in this population. »

# Contraindications for transcatheter aortic valve implantation

## Absolute contraindications
- Absence of a “heart team” and no cardiac surgery on the site.
- Appropriateness of TAVI, as an alternative to AVR, not confirmed by a “heart team”.

### Clinical
- Estimated life expectancy < 1 year.
- Improvement of quality of life by TAVI unlikely because of comorbidities.
- Severe primary associated disease of other valves with major contribution to the patient’s symptoms that can be treated only by surgery.

### Anatomical
- Inadequate annulus size (< 18 mm, > 29 mm).
- Thrombus in the left ventricle.
- Active endocarditis.
- Elevated risk of coronary ostium obstruction (asymmetric valve calcification, short distance between annulus and coronary ostia, small aortic sinuses).
- Plaques with mobile thrombi in the ascending aorta, or arch.
- For transfemoral/subclavian approach: inadequate vascular access (vessel size, calcification, tortuosity).

## Relative contraindications
- Bicuspid or non-calcified valves.
- Untreated coronary artery disease requiring revascularization.
- Haemodynamic instability.
- LVEF < 20%.
- For transapical approach: severe pulmonary disease, LV apex not accessible.

---

**We need evidence in patients with “relative contra indications”**

---

« Treating bioprosthetic failure by transcatheter valve-in-valve implantation cannot be considered as a valid alternative to surgery except in inoperable or high-risk patients as assessed by a ‘heart team’. »
"I'm not here for committing a crime — I'm here for failing to comply with a guideline."
1. Scientific evidence is often lacking (subgroups)

2. Findings may be misleading because of design flaws → bias or poor generalizability

3. Guideline development groups often lack the time, resources, and skills to gather and scrutinise every last piece of evidence

4. Recommendations involve subjective value judgments when the benefits are weighed against the harms

5. What is best for patients overall, may be inappropriate for individuals

6. Guidelines encompass recommendations for which evidence is extrapolated from clinical trials
Aging population: more complex patients

Shortcomings of Guidelines and Risk scores

Heart-team should estimate risk-benefit ratio: cardiac-intensivist involvement

Low flow low gradient AoS: TAVI an alternative
What looks safe

........................................
Patient with severe Aortic Stenosis

75 year old male, EF 55%, no co-morbidities

- STS score: 1%
- Euroscore I: 4%
- Euroscore II: 1%

85 year old female, EF 30%, renal insufficiency, pulmonary hypertension

- STS score: 12%
- Euroscore I: 50%
- Euroscore II: 6%
Newer devices, less complications

Durability issue: both for surgical AVR and TAVI

Heart-team should estimate risk-benefit ratio

Patients first opt for the less invasive option
Advantages Heart-team

One
• Decision-making more accurate according to guidelines

Two
• Team has more knowledge than an individual

Three
• Higher ratings of patients’ experience of care

Four
• Physicians “share the burden”

Five
• Liability

Six
• Increased trial recruitment

Seven
• Adjustment of the limitations of Risk scores
Management of severe aortic stenosis

Severe AS

Symptoms

No

LVEF < 50%

No

Physically active

No

Exercise test

No

Symptoms or fall in blood pressure below baseline

No

Presence of risk factors and low/intermediate individual surgical risk

No

Re-evaluate in 6 months

Yes

Contraindication for AVR

No

High risk for AVR

No

AVR

Yes

AVR or TAVI

Yes

Short life expectancy

No

TAVI

Yes

Med Rx

<table>
<thead>
<tr>
<th></th>
<th>Risk factors not in scores</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>• Hostile chest</td>
</tr>
<tr>
<td>2</td>
<td>• Liver cirrhosis</td>
</tr>
<tr>
<td>3</td>
<td>• Porcelain aorta</td>
</tr>
<tr>
<td>4</td>
<td>• Frailty</td>
</tr>
<tr>
<td>5</td>
<td>• Hospital / surgeon experience</td>
</tr>
</tbody>
</table>
“No off course no Heart team”

Because:

- Time consuming: money!
- We have trials / guidelines
- Heart-team → Delay in treatment
Advancements in TAVI

- Patient assessment
- Imaging
- Cerebral protection devices
- Indications
- Second generation TAVI