LOW FLOW LOW GRADIENT AORTIC STENOSIS

HOW MANY DISEASES ARE WE TALKING ABOUT?
BACKGROUND

• THE LV’s RESPONSE TO PRESSURE OVERLOAD IS WANTONLY CAPRICIOUS.
Primary stimulus

Pressure overload
Increased peak systolic \( \sigma_m \)
Parallel replication of sarcomeres
Wall thickening
CONCENTRIC HYPERTROPHY

Volume overload
Increased end-diastolic \( \sigma_m \)
Series replication of sarcomeres
Chamber enlargement
ECCENTRIC HYPERTROPHY

Beth Israel
• \( \sigma = \frac{P \times r}{2th} \)
80 Y/O WOMAN

- CLASS III Sx OF DYSPNEA
- 3/6 SEM; DELAYED CAROTIDS
- ABSENT A₂
ECHO

- 1.7 cm LV WALL
- EF 0.62
- MEAN GRADIENT 24 mm Hg
- AVA 0.8 cm²
• SMALL THICK VENTRICLES

• NO ROOM FOR THE BLOOD

• LOW STROKE VOL, NL EF

• LOW GRADIENT
WHY CAUSES THIS HETEROGENEITY IN RESPONSE?

STENOSIS SEVERITY?

PATIENT FACTORS (BODY HABITUS, ACTIVITY etc)?

RATE OF ORIFICE NARROWING?

GENETIC BACKGROUND?
CANINE MODEL OF AS

- CONTROLLABLE AORTIC BAND
- DOGS OUTWARDLY SIMILAR
- BROWN, MALE, 25 kg
KOIDE, CARABELLO et al CIRC 1997
IS LVH GOOD OR BAD
YES
WELL-KNOWN

- LVH INCREASES MORTALITY, ESPECIALLY IN THE FACE OF ISCHEMIA
DUNCAN et al. ATS 2008

AVR MORTALITY

- CONC GEO: 38/964 (3.9%)
- NO CONC GEO: 18/964 (1.9%)

MORBIDITY

- 33/964 (3.4%)
- 17/964 (1.8%)
<table>
<thead>
<tr>
<th></th>
<th>Total &quot;tight&quot; TAC</th>
<th>1 day survival</th>
<th>3 day survival</th>
<th>7 day survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>NTG littermates (of 5x-RGS4-myc mice)</td>
<td>9</td>
<td>8 (89%)</td>
<td>7 (78%)</td>
<td>7 (78%)</td>
</tr>
<tr>
<td>NTG C57BL × SJL</td>
<td>48</td>
<td>41 (85%)</td>
<td>30 (63%)</td>
<td>30 (63%)</td>
</tr>
<tr>
<td>5x-RGS4-myc</td>
<td>18</td>
<td>6 (33%)</td>
<td>2 (11%)</td>
<td>2 (11%)</td>
</tr>
<tr>
<td>8x-RGS4-myc</td>
<td>14</td>
<td>2 (14%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

![Graph showing survival over days](image)

Rogers et al  JCI 1999
WHAT IS SEVERE AS
WHEN YOU FIND OUT YOU TELL ME
SEVERE AS
1.0

• WIGGERS EXPERIMENTS IN RUBBER TUBES, CIRCA 1938
40 mm Hg

• 1998 ACC/AHA GUIDELINES: 50 mm Hg
Valve area vs. mean pressure gradient of 3483 echocardiographic studies in patients with aortic valve stenosis and normal left ventricular function.
AND THEN THERE IS INDEXING
AS HAS CHANGED

AND WE CHANGED IT
Figure 28.7 Left ventricular (LV) and femoral artery (FA) pressure tracings in a patient with severe aortic stenosis (aortic valve area 0.4 cm²). During pullback of the retrograde catheter from LV to ascending aorta, the peak systolic femoral artery pressure can be seen to increase (ΔP) by approximately 20 mm Hg. This sign is seen only in patients with aortic valve areas <0.6 cm². The mechanism of this phenomenon is believed to be partial obstruction of an already narrowed aortic orifice by the retrograde catheter and relief of this obstruction with catheter withdrawal. (From Carabello BA, et al. Changes in arterial pressure during left heart pullback in patients with aortic stenosis. Am J Cardiol 1979;44:424.)
• Velocity increases as blood passes through the stenosis
• Pressure Gradient = $4V^2$
Survival (percent) vs. Age (years)

- Latent Period
- Increasing obstruction, myocardial overload
- Symptoms
- Average Age Death

- Age (years): 40, 50, 60, 70, 80
- Survival (percent): 100, 80, 60, 40, 20, 0
RV

\[ \text{PAP} = \text{CO} \times \text{X} \]

PR

\[ \text{Ao valve} \]

BP = CO \times \text{SVR}
TAKING CARE OF THE LOW GRADIENT LOW FLOW SEVERE AS PATIENT

• 1. THE DEFINITION OF SEVERE IS SHAKY

• 2. THE RESPONSE OF THE LV IS MANIFOLD

• 3. IT’S NOT SURPRISING THAT ONE SIZE DOESN’T FIT ALL
72 Y/O MAN

• DYSPNEA WALKING 50 ft. TO GET THE NEWSPAPER IN THE MORNING

• 3 PILLOW ORTHOPNEA

• WITHOUT SYNCOPE OR ANGINA
PE

- BP 110/80 P84
- EST CVP: 10 cm H₂O
- BILAT BASILAR RALES
- 2/6 MID-LATE PEAKING SEM
- CAROTIDS WEAK, ? DELAYED
ECHO

- EF 0.22
- Pk JET vel 2.8 m/sec
- MEAN GRADIENT 22 mm Hg
- AVA 0.9 cm$^2$
- DIMENSIONLESS INDEX 0.27
CARABELLO et al. CIRC, 1980
WHO’S GOING TO DIE?; WHO’S GOING TO GET BETTER?
NOT VERY WORRIED ABOUT THE 35/40 PATIENT
Kaplan-Meier survival estimates by group and treatment.

72 Y/O MAN

- DYSPNEA WALKING 50 ft. TO GET THE NEWSPAPER IN THE MORNING

- 3 PILLOW ORTHOPNEA

- WITHOUT SYNCOPE OR ANGINA
• NEGATIVE INJOTROPIC RESERVE
Le Ven et al. JACC '13
INFUSION OF SNP AT 25 mcg/min
<table>
<thead>
<tr>
<th>Parameter</th>
<th>REST</th>
<th>SNP</th>
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</thead>
<tbody>
<tr>
<td>MAP mmHg</td>
<td>68</td>
<td>62</td>
</tr>
<tr>
<td>CO l/min</td>
<td>3.5</td>
<td>5.0</td>
</tr>
<tr>
<td>Mg mm Hg</td>
<td>20</td>
<td>19</td>
</tr>
<tr>
<td>AVA cm²</td>
<td>0.8</td>
<td>1.2</td>
</tr>
</tbody>
</table>
Overall p value 0.001
Pseudo AS vs. True-severe AS  p value 0.001
Pseudo AS vs. No contractile reserve  p value <0.001

Pseudo AS: 29 patients
True-severe AS: 43 patients
No contractile reserve: 35 patients

Patients at risk
True-severe AS 43 24 18 14 11 6 4
Pseudo AS 29 25 19 14 10 7 5
No contractile reserve 35 15 10 6 1 0 0
80 Y/O WOMAN

- CLASS III Sx OF DYSPNEA
- 3/6 SEM; DELAYED CAROTIDS
- ABSENT A₂
ECHO

• 1.7 cm LV WALL

• EF 0.62

• MEAN GRADIENT 24 mm Hg

• AVA 0.8 cm$^2$
NORMAL EF BUT NOT NORMAL SYSTOLIC FUNCTION
• NORMAL SARCOMERE SHORTENING IS 0.10-0.12%

• NORMAL EF IS 0.60
• SUBNORMAL SARCOMERE SHORTENING CAN STILL YIELD A NORMAL EF
BAICU, ZILE et al. CIRC: 2005
SEVERE LOW GRADIENT NL  EF AS
TALK ABOUT APPLES AND FREIGHT TRAINS
STUDY MISCONSTRUCTIONS

• COMPARING SYMPTOMATIC TO ASYMPTOMATIC PATIENTS

• ADMIXING CAD AND THOSE WITH CLEAN CORONARIES

• USING AVA ALONE TO DEFINE AS
DOES THE Pt REALLY HAVE SEVERE AS TO BEGIN WITH
Figure 1. Individual and median changes in mean Doppler gradient (A) and peak aortic jet velocity (B) showing significant increase for both parameters compared to baseline (p <0.001). Dark solid lines represent median changes.

Christophe Tribouilloy, Dan Rusinaru, Vincent Charles, Jamila Boulif, Frédéric Maes, Franck Lévy, Agnès Pasquet, Sylvestre Maréchaux, Jean-Louis Vanoverschelde

**Progression of Low-Gradient, Low-Flow, Severe Aortic Stenosis With Preserved Left Ventricular Ejection Fraction**


http://dx.doi.org/10.1016/j.amjcard.2015.05.023
Figure 3. Kaplan-Meier survival curves comparing cardiovascular survival in patients with mild or no AS (short dashed line), moderate AS (medium dashed line), severe paradoxical LG-AS (dashed and dotted line), and severe HG-AS (solid line). Numbers at bottom i...

Nawel Rezzoug, Bert Vaes, Agnès Pasquet, Bernhard Gerber, Christophe de Meester, Gijs Van Pottelbergh, Wim Adriaensen, Catharina Matheï, Jan DeGryse, Jean-Louis Vanoverschelde

**Prevalence and Prognostic Impact of Valve Area—Gradient Patterns in Patients ≥80 Years With Moderate-to-Severe Aortic Stenosis (from the Prospective BELFRAIL Study)**

The American Journal of Cardiology, Volume 116, Issue 6, 2015, 925–932

http://dx.doi.org/10.1016/j.amjcard.2015.05.062
• MODERATE AS USING ONLY AVA FOR DEFINITION

• ALL AS IS NOT ALIKE
IT’S ALL GOT TO FIT

• PHYSICAL EXAM
• AVA, JET
• VALVE MOVEMENT
• CALCIFICATION
Figure 1. Distribution of Aortic Valve Calcification by Sex in the Various AS Groups
Concordant grading-moderate aortic stenosis (AS), discordant grading with low mean gradient (MG), discordant grading with high MG, and concordant grading-severe AS; x-axis in b...

Marie-Annick Clavel, David Messika-Zeitoun, Philippe Pibarot, Shivani R. Aggarwal, Joseph Malouf, Phillip A. Araoz, Hector I. Michelen, Caroline Cueff, Eric Larose, Romain Capoulade, Alec Vahanian, Maurice Enriquez-Sarano

The Complex Nature of Discordant Severe Calcified Aortic Valve Disease Grading: New Insights From Combined Doppler Echocardiographic and Computed Tomographic Study


http://dx.doi.org/10.1016/j.jacc.2013.08.1621
• YOU CAN NEVER COMPARE ASYMPTOMATIC PATIENTS TO SYMPTOMATIC PATIENTS NO MATTER WHAT THE AVA
LOW FLOW, LOW GRADIENT
SEVERE AS IS REAL
Kaplan–Meier all-cause mortality analysis to 2 years is shown for patients with low flow (LF) vs normal flow (NF; A), LF with low ejection fraction (LEF) vs normal ejection fraction (NEF; B), and LF with LEF and low gradient (LG) vs normal gradient (NG; C).

Figure 4. Baseline and 9-Month Follow-Up of Mitral Ring Displacement Data According to the 4 Groups Studied

Patients with moderate AS showed higher values both at baseline and follow-up compared with patients with low-gradient AS, irrespective of ejection fract...

Sebastian Herrmann, Stefan Störk, Markus Niemann, Volkmar Lange, Jörg M. Strotmann, Stefan Frantz, Meinrad Beer, Stefan Gattenlöhner, Wolfram Voelker, Georg Ertl, Frank Weidemann

http://dx.doi.org/10.1016/j.jacc.2011.02.059
Figure 3  Kaplan–Meier Curves of Overall Survival According the Group of Patients and Type of Treatment  Kaplan–Meier curves of overall survival according the group of patients and type of treatment: AVR versus Conservative (Cons). Abbreviations a...

Marie–Annick Clavel, Jean G. Dumesnil, Romain Capoulade, Patrick Mathieu, Mario Sénéchal, Philippe Pibarot

Outcome of Patients With Aortic Stenosis, Small Valve Area, and Low–Flow, Low–Gradient Despite Preserved Left Ventricular Ejection Fraction

Journal of the American College of Cardiology Volume 60, Issue 14 2012 1259 – 1267

http://dx.doi.org/10.1016/j.jacc.2011.12.054
Figure 6. Kaplan-Meier survival plot for overall survival of the three different groups. Note the worst survival in AS patients with LF/LG physiology.

Sebastian Herrmann, Bastian Fries, Dan Liu, Kai Hu, Stefan Stoerk, Wolfram Voelker, Catharina Ruppert, Kristina Lorenz, Georg Ertl, Frank Weidemann

**Differences in Natural History of Low- and High-Gradient Aortic Stenosis from Nonsevere to Severe Stage of the Disease**

Journal of the American Society of Echocardiography, 2015, Available online 28 August 2015

http://dx.doi.org/10.1016/j.echo.2015.07.016
Figure 2. Kaplan-Meier Curves for Clinical Outcomes According to Assigned Treatment Modality

Kaplan-Meier analysis of death (A) and cardiovascular death (B) at 1 year according to the assigned treatment modality. Abbreviations as in Figure 1.

Crochan J. O’Sullivan, Lars Englberger, Nicola Hosek, Dik Heg, Davide Cao, Giulio G. Stefanini, Stefan Stortecky, Steffen Gloekler, Ernest Spitzer, David Tüller, Christoph Huber, Thomas Pilgrim, Fabien Praz, Lutz Buellesfeld, Ahmed A. Khattab, Thierry Carrel, Bernhard Meier, Stephan Windecker, Peter Wenaweser

Clinical Outcomes and Revascularization Strategies in Patients With Low-Flow, Low-Gradient Severe Aortic Valve Stenosis According to the Assigned Treatment Modality

JACC: Cardiovascular Interventions, Volume 8, Issue 5, 2015, 704–717

http://dx.doi.org/10.1016/j.jcin.2014.11.020
Figure 4. Kaplan-Meier Curves for Clinical Outcomes Stratified by Completeness of Revascularization Among TAVR and SAVR Patients Only

Kaplan-Meier analysis of death (A) and cardiovascular death (B) at 1 year according to the completeness of revascularization am...

Crochan J. O'Sullivan, Lars Englberger, Nicola Hosek, Dik Heg, Davide Cao, Giulio G. Stefanini, Stefan Stortecky, Steffen Gloekler, Ernest Spitzer, David Tüller, Christoph Huber, Thomas Pilgrim, Fabien Praz, Lutz Buellesfeld, Ahmed A. Khattab, Thierry Carrel, Bernhard Meier, Stephan Windecker, Peter Wenaweser

Clinical Outcomes and Revascularization Strategies in Patients With Low-Flow, Low-Gradient Severe Aortic Valve Stenosis According to the Assigned Treatment Modality

JACC: Cardiovascular Interventions, Volume 8, Issue 5, 2015, 704–717

http://dx.doi.org/10.1016/j.jcin.2014.11.020
AND IF SYMPTOMATIC MUST BE TREATED AS SUCH
SUMMARY

• LOW FLOW LOW GRADIENT LOW EF AORTIC STENOSIS IS THE PRODUCT OF A VERY SICK HEART, ESPECIALLY 20/20.

• INOTROPIC RESERVE IS IMPORTANT IN SURGICAL RISK STRATIFICATION BUT NOT IN PREDICTING POST-OP OUTCOME

• BAV MAY BE A USEFUL BRIDGE IN SUCH PATIENTS
LOW FLOW NORMAL EF SEVERE AORTIC STENOSIS

• MAKE SURE THEY’VE GOT IT

• PROGNOSIS REDUCED BUT BETTER OUTCOME WITH AVR. ? TAVR
SINGLE MOST IMPORTANT GUIDELINES

• HEART TEAM

• INTEGRATIVE APPROACH
• IF YOU FOLLOW THESE GUIDELINES WITHOUT FAIL
YOU’RE NOT DOING YOUR JOB