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Aortic Stenosis Severity is Universally Under-estimated in Atrial Fibrillation: Time to Change the Guidelines

Said Alsidawi, MD
Assistant Professor of Medicine and Consultant
Mayo Clinic School of Medicine
Director, Hypertrophic Cardiomyopathy Program
Co-Chair, Research Unit and Clinical Trials
Department of Cardiovascular Disease

MHI Grand Rounds
3/10/2025

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Objectives:

1. Outline how atrial fibrillation complicates the assessment of aortic stenosis

2. Review available data that supports the universal underestimation of aortic stenosis in patients with atrial fibrillation

3. Propose a new contemporary approach to assess aortic stenosis severity when accompanied by atrial fibrillation

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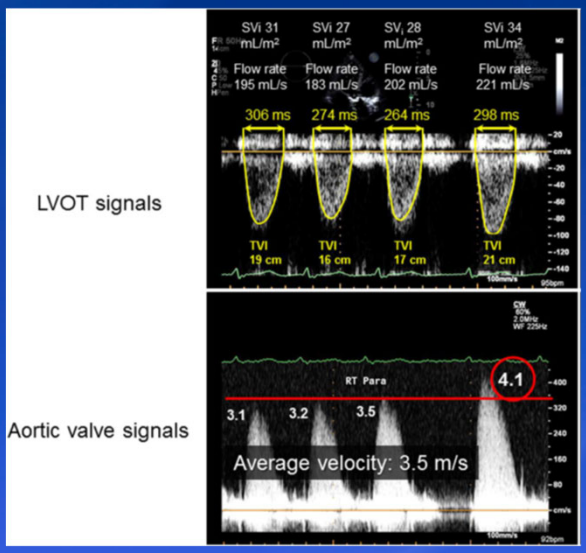
AF



Data From: Alsidawi et al *Circ Cardiovasc Imaging*. 2021;14:e012453

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How bad is the AS

1. Severe
2. Not severe
3. It depends

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aortic stenosis

	Aortic Jet Velocity (m/s)	Mean Gradient (mmHg)	Valve Area (cm^2)
Normal	≤2.0	<5	3.0–4.0
Mild	<3.0	<25	>1.5
Moderate	3.0–4.0	25–40	1.0–1.5
Severe	>4.0	>40	<1.0

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Nishimura et al. Circ 2014

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Table 4: Calcium Score by Computed Tomography in Grading of Aortic Stenosis

	Men	Women
Severe aortic stenosis very likely	≥3,000	≥1,600
Severe aortic stenosis likely	≥2,000	≥1,200
Severe aortic stenosis unlikely	<1,600	<800

Source: Baumgartner, et al., 2017.[24]

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Computed tomography aortic valve calcium scoring for the assessment of aortic stenosis progression

Mhairi Katrina Doris,[1] William Jenkins,[1] Philip Robson,[2] Tania Pawade,[1] Jack Patrick Andrews,[1] Rong Bing,[1] Timothy Cartlidge,[1] Anoop Shah,[1] Alice Pickering,[1] Michelle Claire Williams,[1,3] Zahi A Fayad,[2] Audrey White,[1] Edwin JR van Beek,[1,3] David E Newby,[1] Marc R Dweck[1]

Average change in AV CS was 152 AU/year

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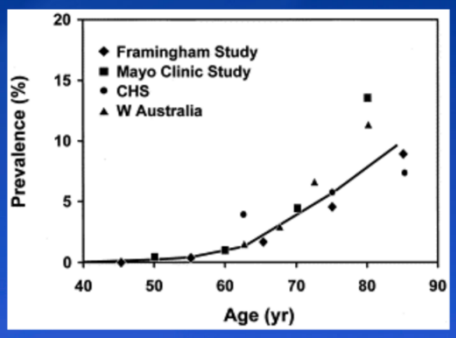
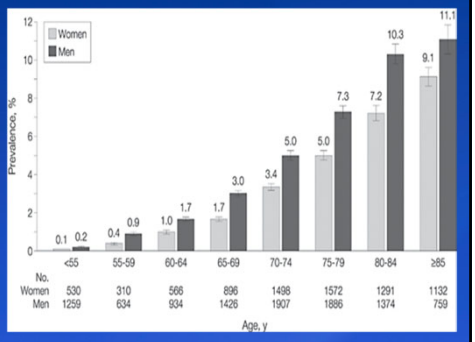
Prevalence of AF by age:





Chugh et al. JACC 2001

Go et al. JAMA 2001

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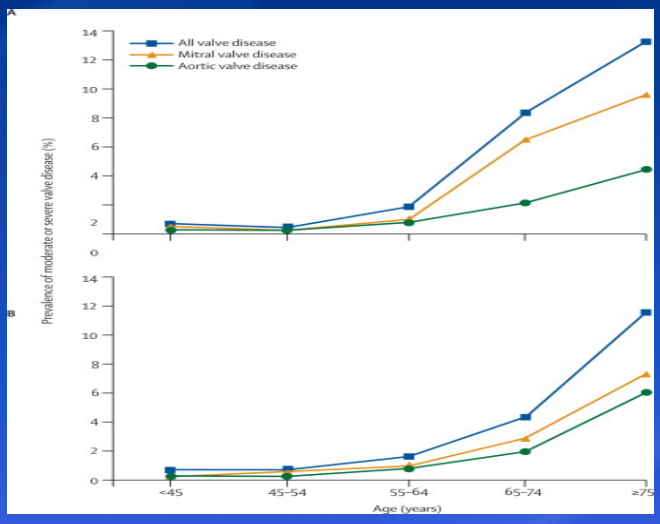
Prevalence of AS by age:



Nkomo et al. Lancet 2006

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Prevalence of AF in AS patients

- AF in general affects 1-2 % of the general population (Chugh 2001)
- It affects 9% of patient with moderate AS with an incidence of 1.2%/year (Greve 2013).
- In patients referred for TAVR in the French database, 26% had AF at time of referral (Chopard 2015) And 37% in PARTNER I trial (Biviano 2016)
- And up to 35-50% in patients with LFLG AS with reduced EF (Levy 2006, Eleid 2012)

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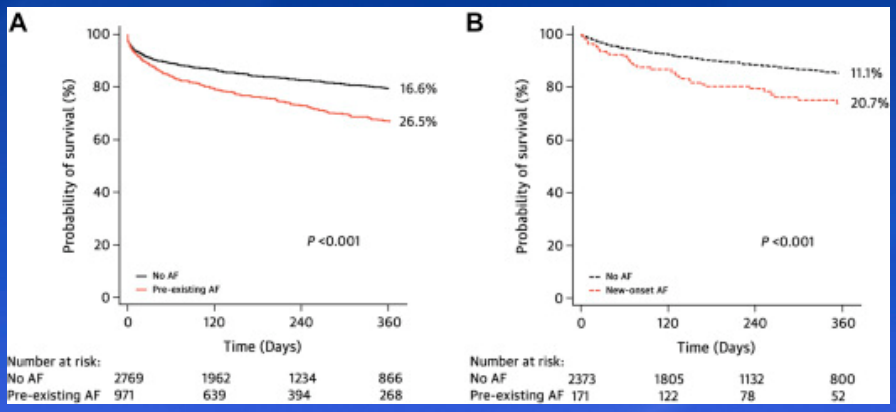
Is AF bad in patient with AS?



Chopard et al. JACC Interv 2015

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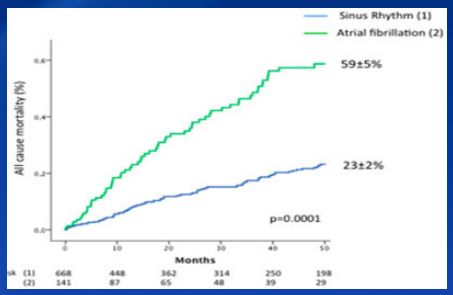
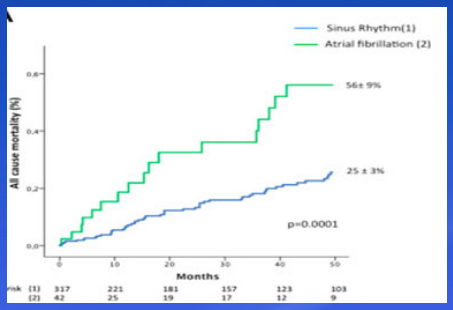
Severe AS



Asymptomatic Severe AS



Levy et al. AJC 2015

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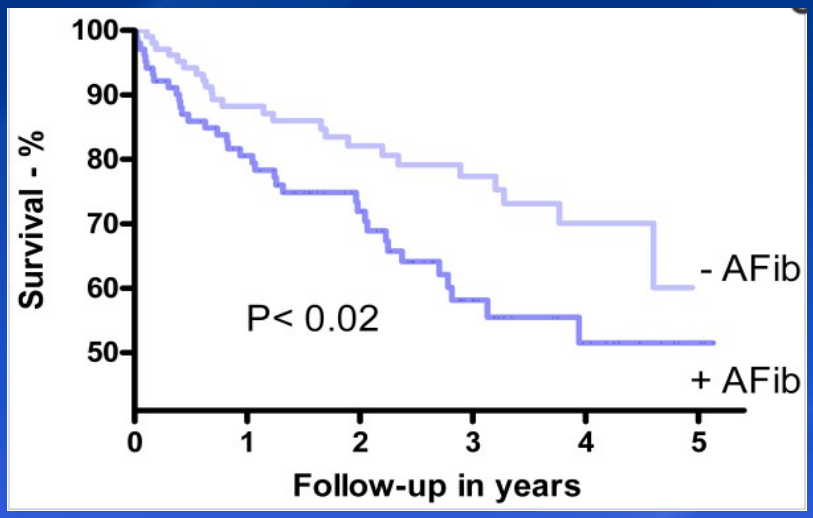
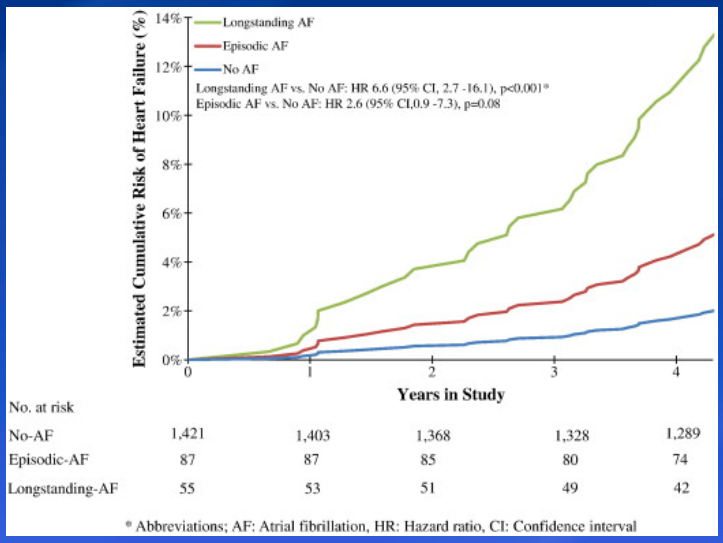
All comers with AS



Burup et al. Cardiovac Ultra. 2012

14

Morbidity in mild-moderate AS



No. at risk					
No-AF	1,421	1,403	1,368	1,328	1,289
Episodic-AF	87	87	85	80	74
Longstanding-AF	55	53	51	49	42

* Abbreviations; AF: Atrial fibrillation, HR: Hazard ratio, CI: Confidence interval

Greve et al. IJC 2013

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Why is this?

- Does atrial fibrillation carry an increased risk of morbidity and mortality in and of itself?
- Does it implicate a more advanced cardiac disease?
- Are we under-referring patients for a timely aortic valve replacement because we are under-estimating the severity of AS?

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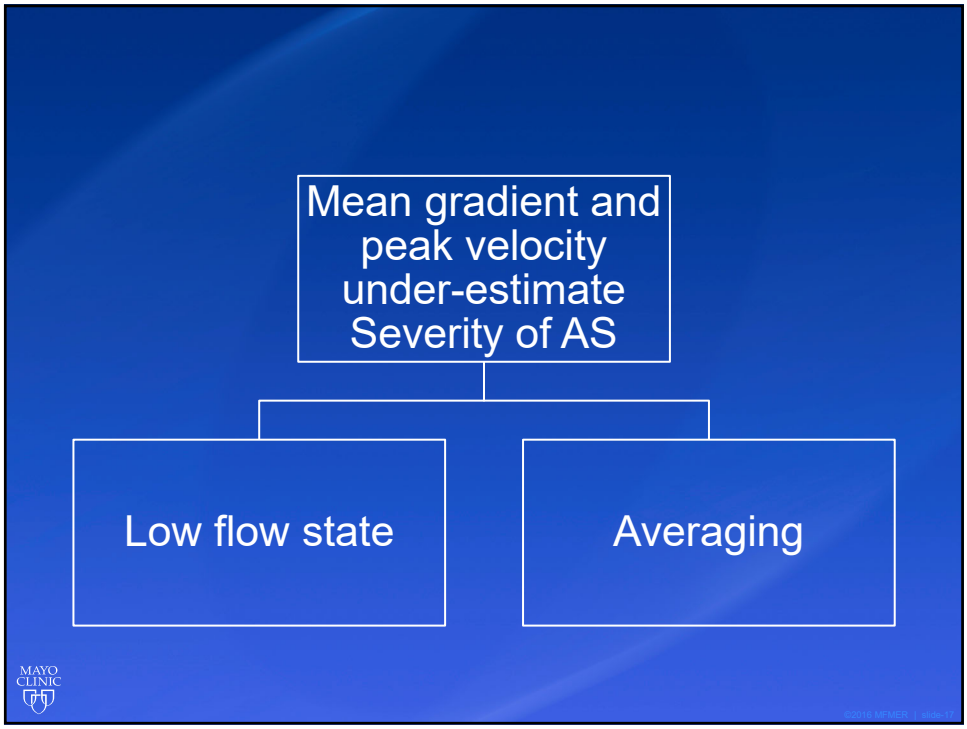
Mean gradient and peak velocity under-estimate Severity of AS
Low flow state
Averaging
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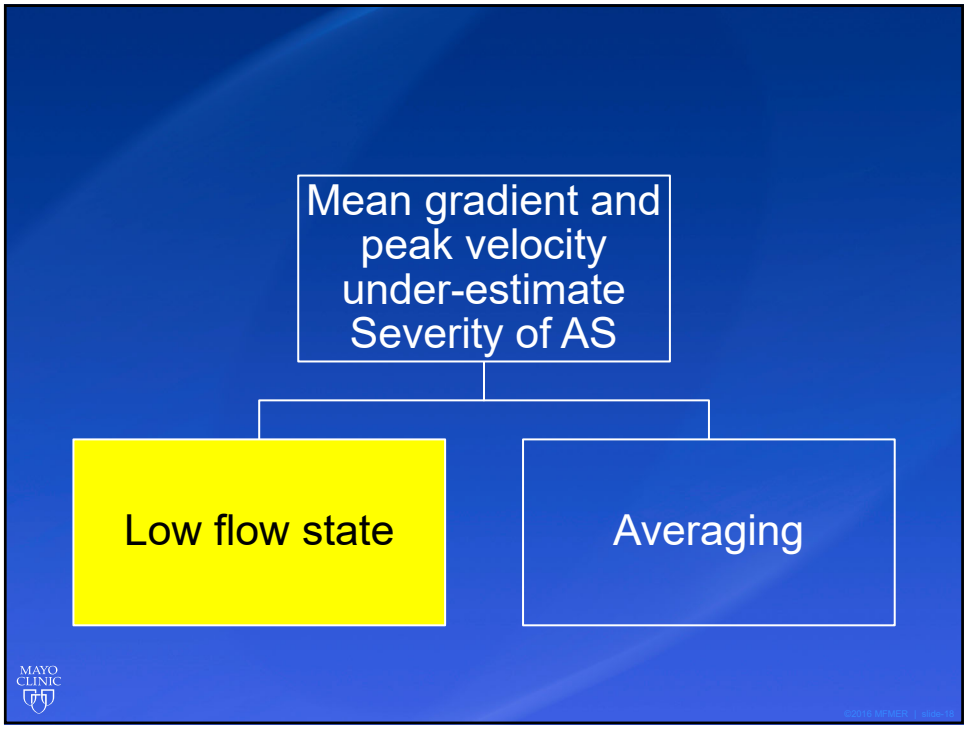
Mean gradient and peak velocity under-estimate Severity of AS
Low flow state
Averaging
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	Group 1, LF/HG (n=50, 3%)	Group 2, LF/LG (n=53, 3%)	Group 3, NF/LG (n=352, 21%)	Group 4, NF/HG (n=1249, 73%)	*P* Value
Age, y	76±14	77±12	80±11†	77±12‡	0.0009
Female sex, n (%)	13 (26)	18 (34)	203 (58)*†	519 (42)‡	<0.0001
Body mass index, kg/m²	35.6±7.5	31.5±8.4*	27.8±5.5*†	28.8±6.0*†‡	<0.0001
Body surface area, m²	2.17±0.25	2.01±0.24*	1.82±0.22*†	1.92±0.24*†‡	<0.0001
Symptoms					
Any symptoms, n (%)	40 (80)	41 (77)	188 (53)*†	924 (74)‡	<0.0001
Dyspnea, n (%)	39 (78)	32 (60)	167 (47)*†	816 (65)‡	<0.0001
Angina, n (%)	4 (8)	12 (23)	45 (13)	227 (18)‡	0.01
Syncope, n (%)	4 (8)	5 (9)	11 (3)	67 (5)	0.12
NYHA class	2.5±0.9	2.0±0.8*	1.9±0.8*	2.1±0.8*‡	<0.0001
Comorbidities and laboratory values					
Atrial fibrillation history, n (%)	16 (32)	27 (51)	69 (20)*†	173 (14)*†	<0.0001
Obesity, n (%)	39 (78)	25 (47)*	102 (29)*†	454 (36)*†‡	<0.0001
Hypertension, n (%)	35 (70)	42 (79)	289 (82)†	884 (71)‡	0.0001
Previous CAD, n (%)	12 (24)	23 (43)*	143 (41)*	294(24)†‡	<0.0001
Previous PCI, n (%)	7 (14)	8 (15)	45 (13)	154 (12)	0.93
Previous CABG, n (%)	9 (18)	4 (8)	46 (13)	174 (14)	0.41
Diabetes mellitus, n (%)	28 (56)	26 (49)	165 (47)	503 (40)*	0.03

Eleid et al. Cric 2013

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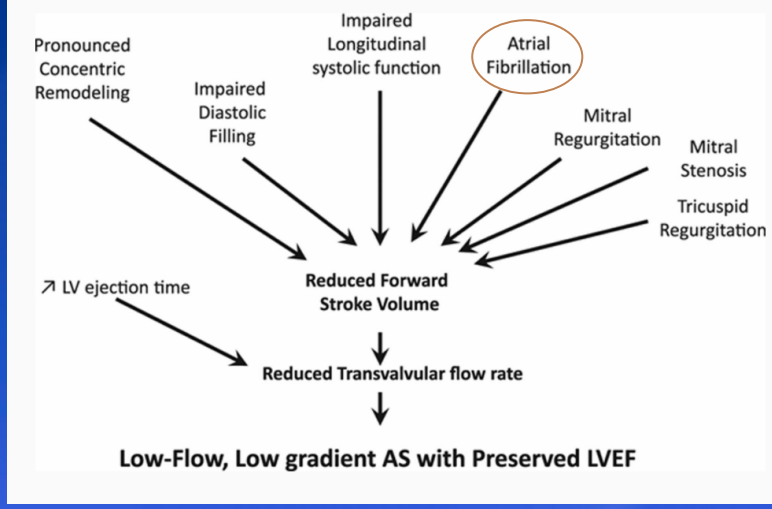

Pibarot et al. Circ 2013

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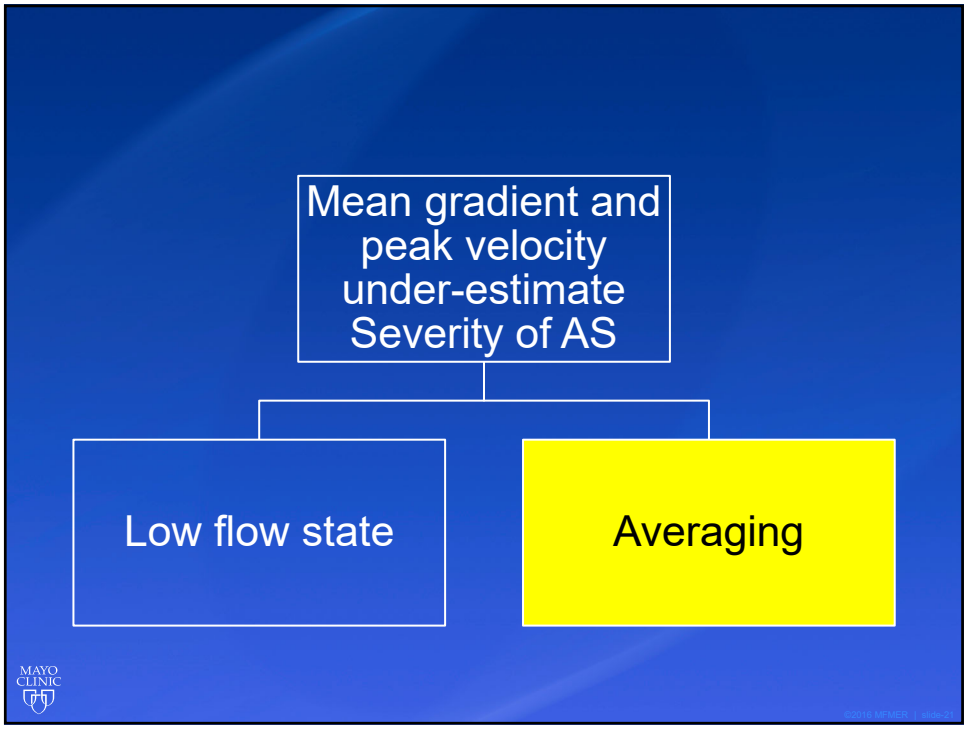
Mean gradient and peak velocity under-estimate Severity of AS
Low flow state
Averaging
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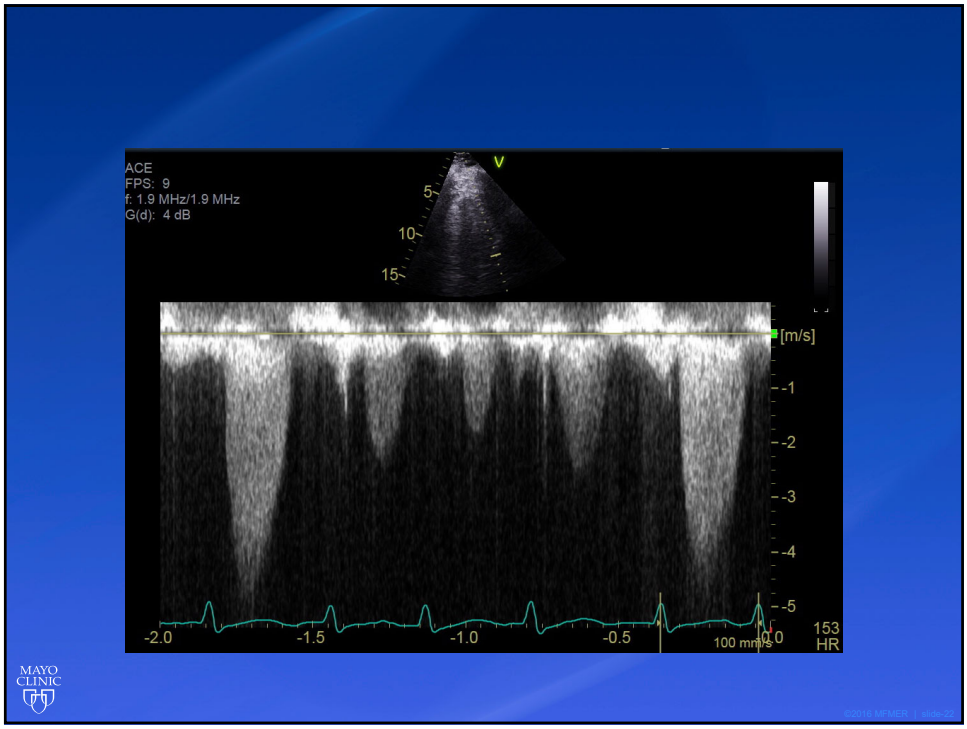
ACE
FPS: 9
f: 1.9 MHz/1.9 MHz
G(d): 4 dB
5
10
15
[m/s]
-1
-2
-3
-4
-5
-2.0
-1.5
-1.0
-0.5
0.0
100 mm/s
153
HR
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GUIDELINES AND STANDARDS

Echocardiographic Assessment of Valve Stenosis: EAE/ASE Recommendations for Clinical Practice

Heart rate at which gradients are measured should always be reported. In patients with atrial fibrillation, mean gradi ent should be calculated as the average of five cycles with the least variation of R–R intervals and as close as possible to normal heart rate.

- Expert consensus.

Baumgartner et al. JASE 2014

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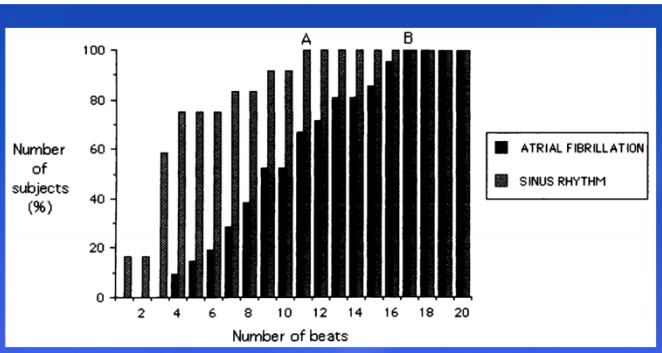
Optimal Number of Beats for the Doppler Measurement of Cardiac Output in Atrial Fibrillation

Simon W. Dubrey, MD, and Rodney H. Falk, MD, *Boston, Massachusetts*

This study was undertaken to determine the optimum number of Doppler velocity waveforms required to calculate cardiac output in atrial fibrillation with the same degree of accuracy as that for sinus rhythm. Twenty-one patients in atrial fibrillation underwent calculations of cardiac output derived from aortic Doppler waveform velocity time integrals and RR intervals. The variability in estimates of the cardiac output was calculated with the successive addition of sequential beats and compared with that determined in a control group of 12 subjects in sinus rhythm. For the group in atrial fibrillation, a mean of 13 beats (range 4 to 17 beats) was required to achieve an estimation of cardiac output with a variability of less than 2%, compared with a mean of four beats in sinus rhythm. In atrial fibrillation, the mean number of beats required to determine cardiac output was approximately three times that necessary in sinus rhythm. (J Am Soc Echocardiogr 1997;10:67-71.)



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Case 1:

- 73-year-old patient with known aortic valve stenosis and persistent AF.
- Referred to Valve Clinic for an opinion on her AS.

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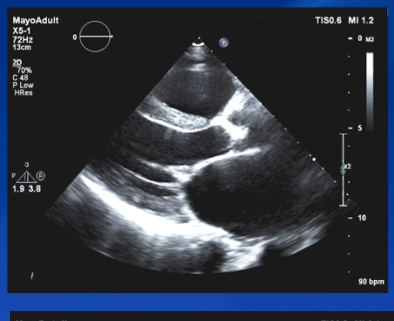

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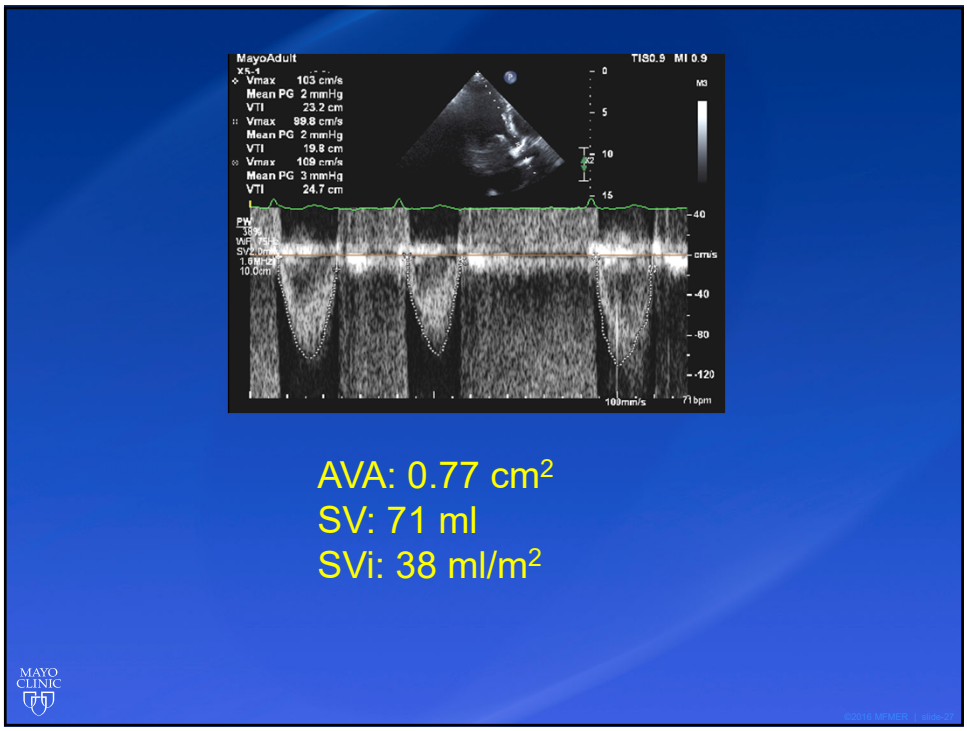
MayoAdult
TIS0.9 MI 0.9
Vmax 103 cm/s
Mean PG 2 mmHg
VTI 23.2 cm
Vmax 99.8 cm/s
Mean PG 2 mmHg
VTI 19.8 cm
Vmax 109 cm/s
Mean PG 3 mmHg
VTI 24.7 cm
100mm/s
71 bpm
AVA: 0.77 cm2
SV: 71 ml
SVi: 38 ml/m2
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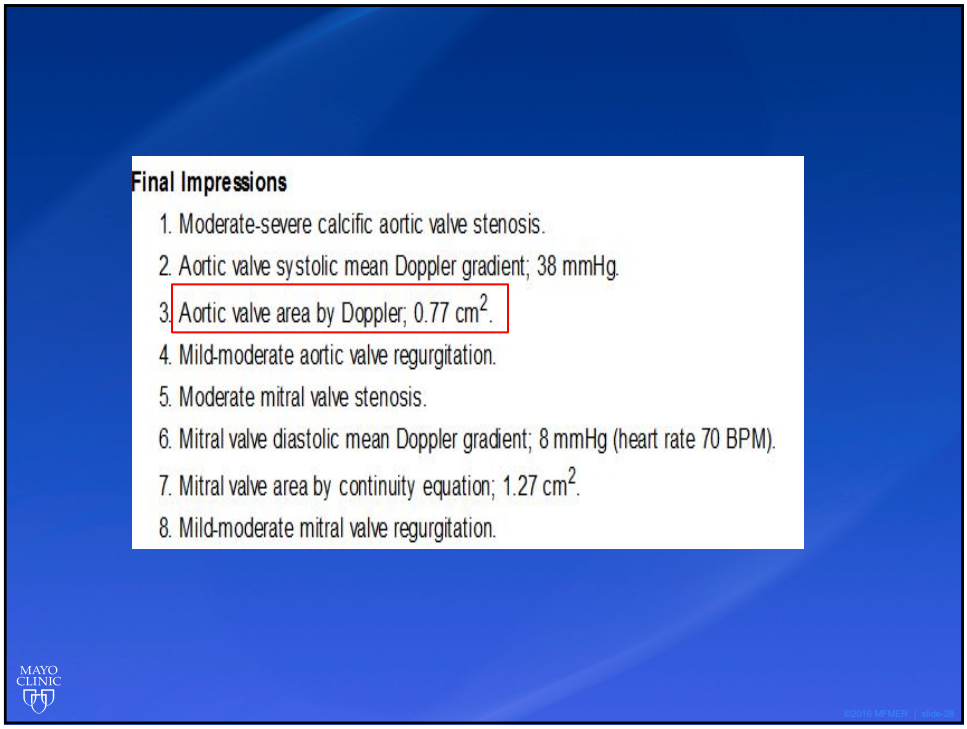
Final Impressions
1. Moderate-severe calcific aortic valve stenosis.
2. Aortic valve systolic mean Doppler gradient; 38 mmHg.
3. Aortic valve area by Doppler; 0.77 cm2.
4. Mild-moderate aortic valve regurgitation.
5. Moderate mitral valve stenosis.
6. Mitral valve diastolic mean Doppler gradient; 8 mmHg (heart rate 70 BPM).
7. Mitral valve area by continuity equation; 1.27 cm2.
8. Mild-moderate mitral valve regurgitation.
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- She was referred from Valve Clinic for a surgical evaluation.
- Surgery gave the patient the option of surgery vs 3 months follow-up. She chose to follow-up.
- Presented to ER with sudden cardiac death after one month.

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Case 2:

- 68-year-old male referred to Valve Clinic for evaluation of aortic valve stenosis.
- He noted significant decline in his exercise tolerance over the last 6 months.
- He has known chronic atrial fibrillation.
- His exam was consistent with severe aortic stenosis.

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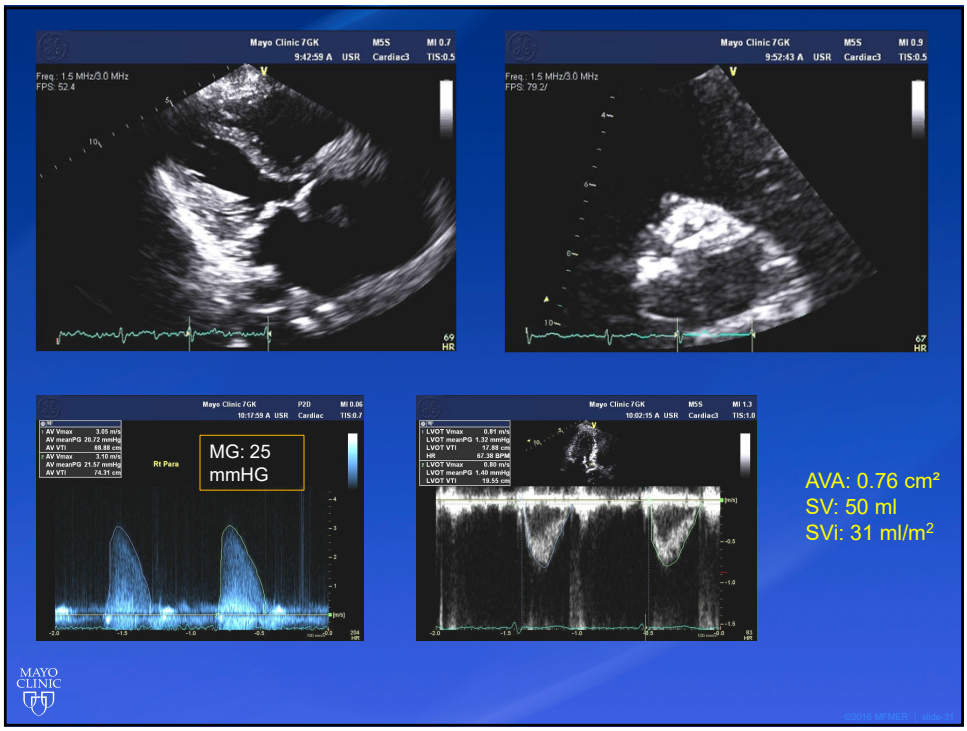

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- Report:

Moderate aortic valve stenosis, maybe moderate-severe. MG: 25 mmHg.

- He was sent for CT calcium scoring which came back 2815.

- He underwent aortic valve replacement.

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- These examples raise 2 questions:

1. Should we average?

2. Can we use the highest signal?

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Circulation: Cardiovascular Imaging

ORIGINAL ARTICLE

High Prevalence of Severe Aortic Stenosis in Low-Flow State Associated With Atrial Fibrillation

Said Alsidawi, MD; Sana Khan, MD; Sorin V. Pislaru, MD, PhD; Jeremy J. Thaden, MD; Edward A. El-Am, MD; Christopher G. Scott, MS; Kareem Morant, MD; Didem Oguz, MD; Sushil A. Luis, MBBS; Ratnasari Padang, MBBS, PhD; Colleen E. Lane, MD; Robert B. McCully, MD; Patricia A. Pellikka, MD; Jae K. Oh, MD; Vuyisile T. Nkomo, MD, MPH

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- Jan 2012 - Dec 2016 (5 years)
- 1541 patients with aortic stenosis
  - AVA ≤ 1 cm^2
  - LVEF ≥ 50%
- What is the significance of single-high Doppler signals meeting criteria for severe AS in LGAS associated with AF?
- Are there any differences in aortic valve calcium scores in AF vs SR in HGAS and LGAS?

Data From: Alsidawi et al *Circ Cardiovasc Imaging*. 2021;14:e012453

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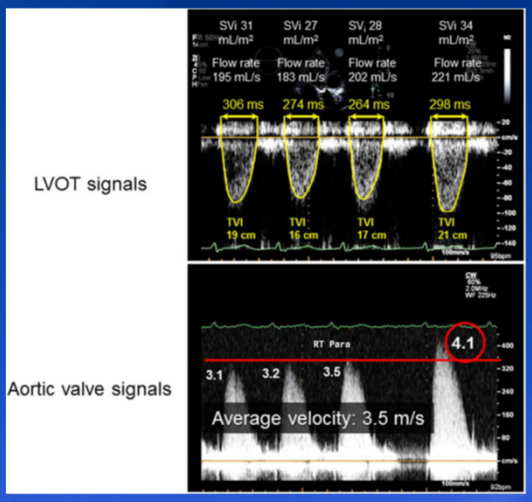

Data From: Alsidawi et al *Circ Cardiovasc Imaging*. 2021;14:e012453

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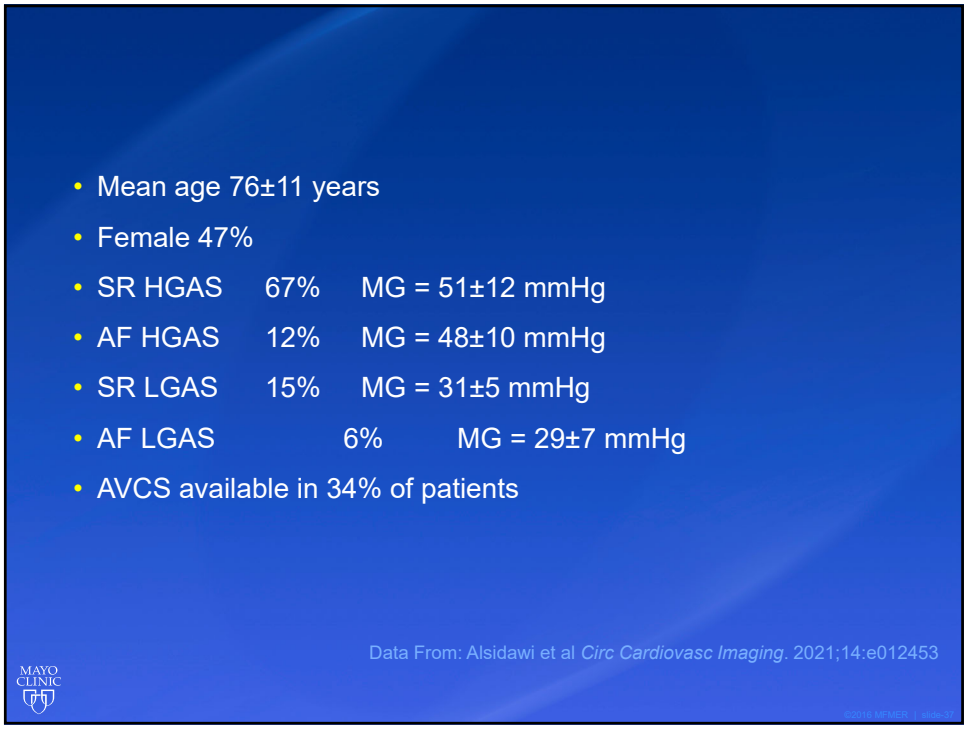
• Mean age 76±11 years
• Female 47%
• SR HGAS 67% MG = 51±12 mmHg
• AF HGAS 12% MG = 48±10 mmHg
• SR LGAS 15% MG = 31±5 mmHg
• AF LGAS 6% MG = 29±7 mmHg
• AVCS available in 34% of patients
Data From: Alsidawi et al Circ Cardiovasc Imaging. 2021;14:e012453
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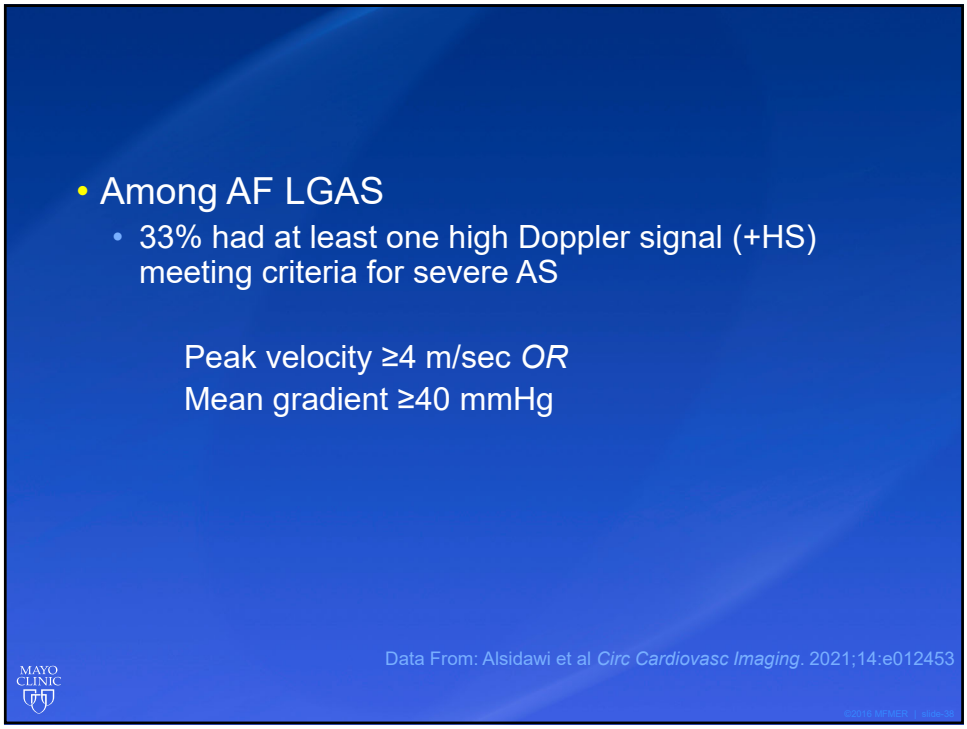
• Among AF LGAS
• 33% had at least one high Doppler signal (+HS) meeting criteria for severe AS
Peak velocity ≥4 m/sec OR
Mean gradient ≥40 mmHg
Data From: Alsidawi et al Circ Cardiovasc Imaging. 2021;14:e012453
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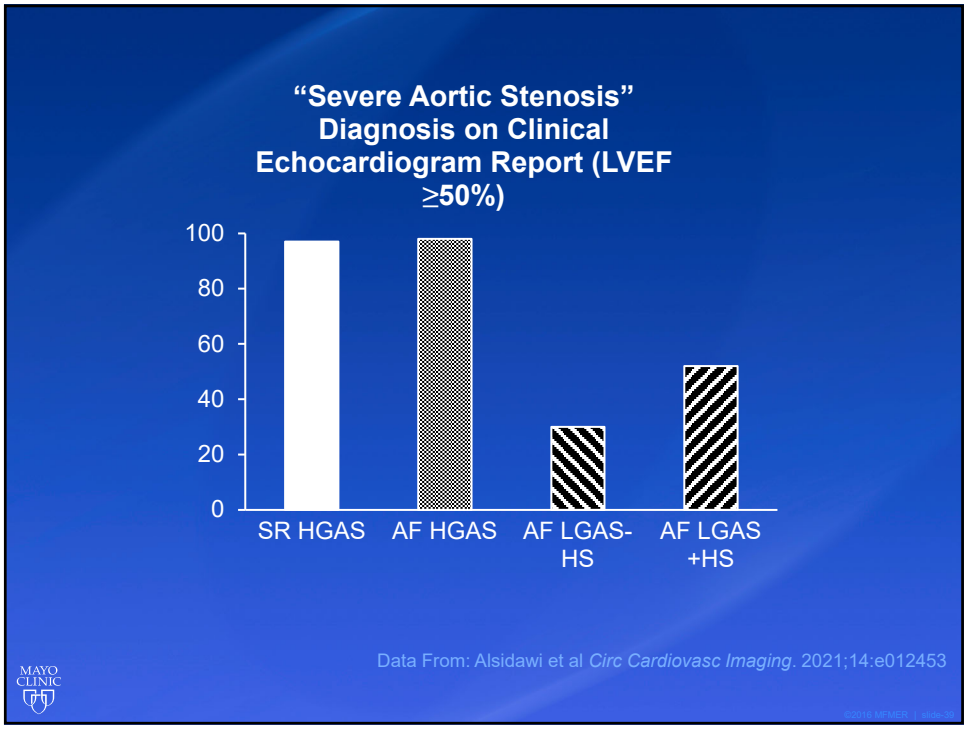
"Severe Aortic Stenosis" Diagnosis on Clinical Echocardiogram Report (LVEF ≥50%)
100
80
60
40
20
0
SR HGAS
AF HGAS
AF LGAS-HS
AF LGAS +HS
Data From: Alsidawi et al Circ Cardiovasc Imaging. 2021;14:e012453

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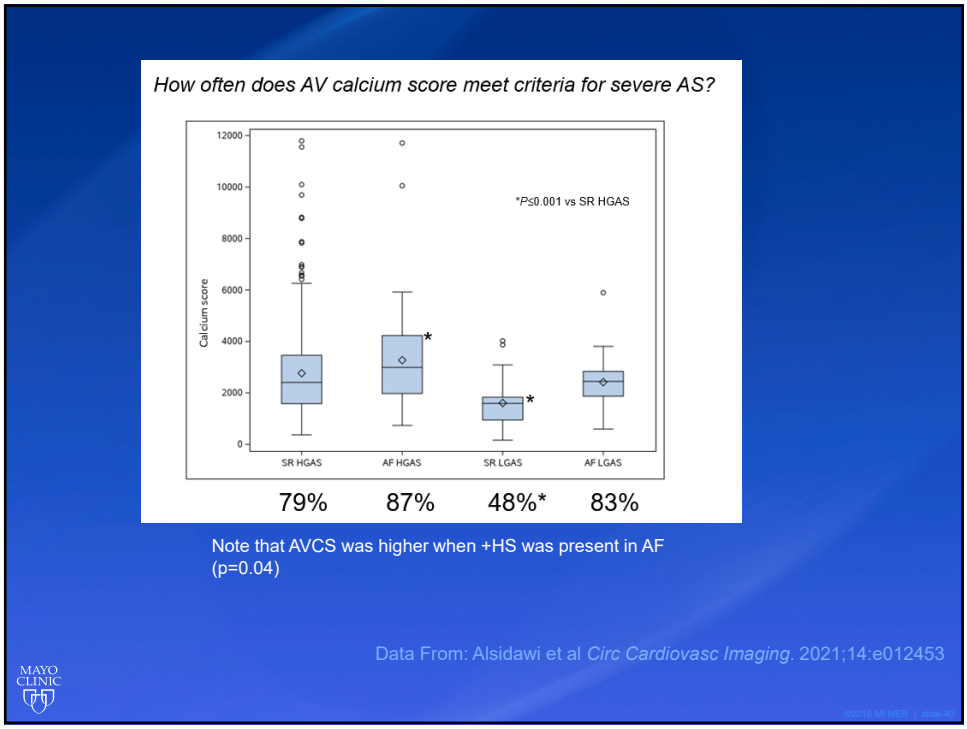
How often does AV calcium score meet criteria for severe AS?
Calcium score
12000
10000
8000
6000
4000
2000
0
*P≤0.001 vs SR HGAS
SR HGAS
AF HGAS
SR LGAS
AF LGAS
79%
87%
48%*
83%
Note that AVCS was higher when +HS was present in AF (p=0.04)
Data From: Alsidawi et al Circ Cardiovasc Imaging. 2021;14:e012453

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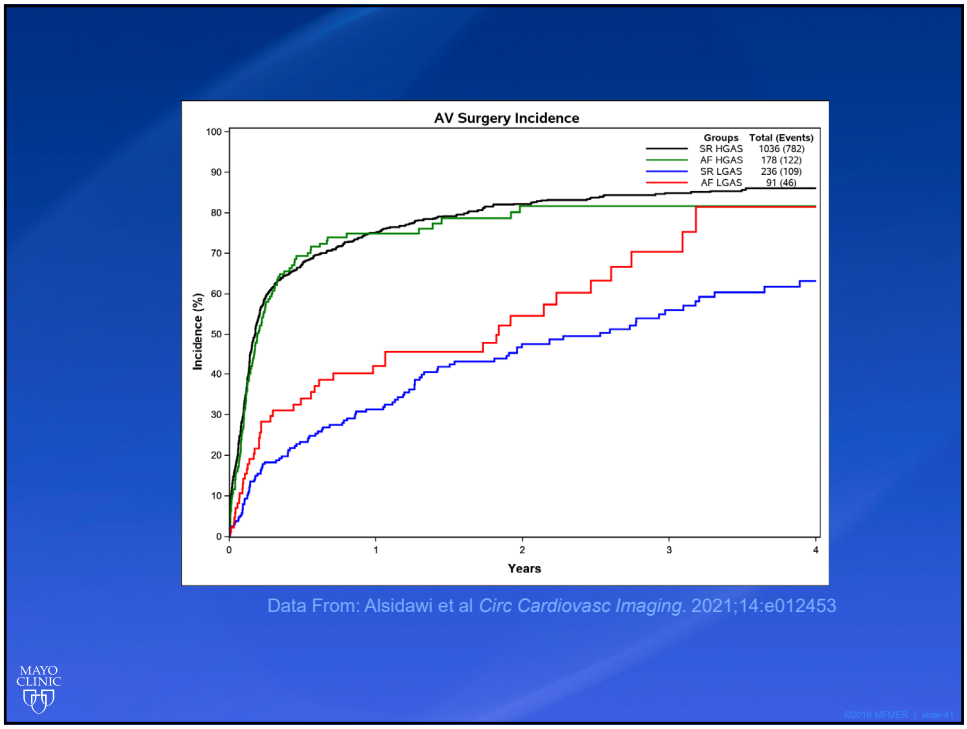
AV Surgery Incidence
Groups Total (Events)
SR HGAS 1036 (782)
AF HGAS 178 (122)
SR LGAS 236 (109)
AF LGAS 91 (46)
Incidence (%)
Years
Data From: Alsidawi et al Circ Cardiovasc Imaging. 2021;14:e012453
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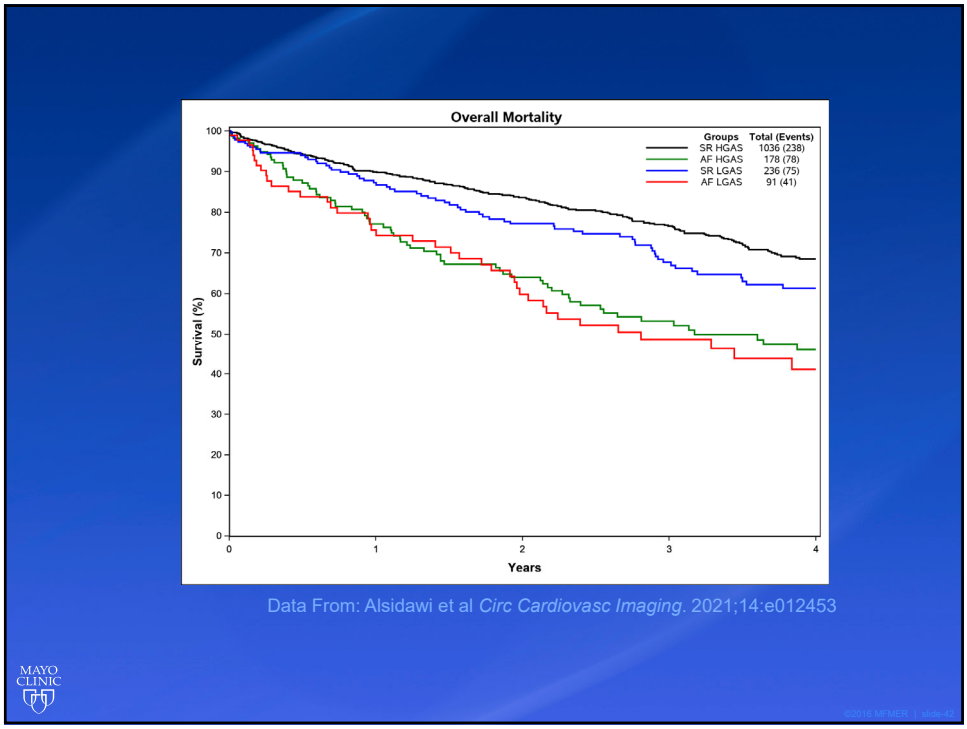
Overall Mortality
Groups Total (Events)
SR HGAS 1036 (238)
AF HGAS 178 (78)
SR LGAS 236 (75)
AF LGAS 91 (41)
Survival (%)
Years
Data From: Alsidawi et al Circ Cardiovasc Imaging. 2021;14:e012453
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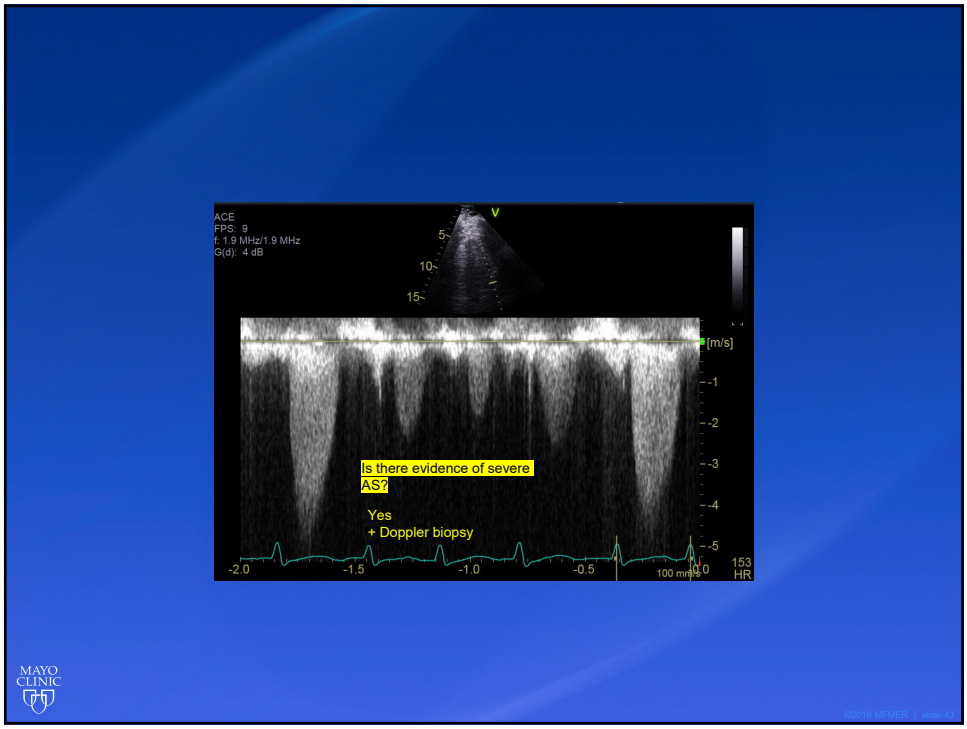
ACE
FPS: 9
f: 1.9 MHz/1.9 MHz
G(d): 4 dB
[m/s]
Is there evidence of severe AS?
Yes
+ Doppler biopsy
153
HR
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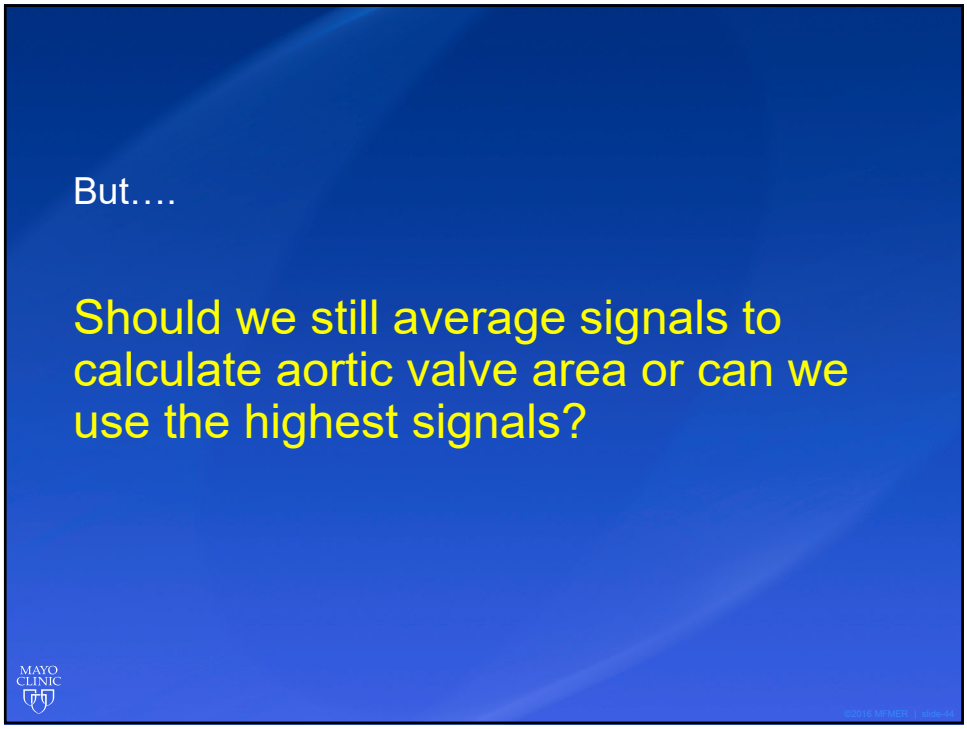
But….
Should we still average signals to calculate aortic valve area or can we use the highest signals?
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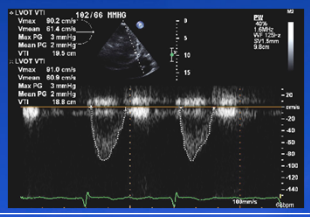
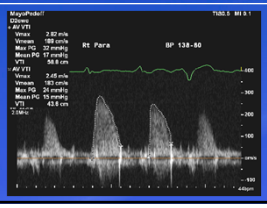
AVA in AF:

- AVA = $\frac{\text{LVOT area} \times \text{Avg. TVI LVOT}}{\text{Avg. TVI AV}}$



- AVA = $\frac{\text{LVOT area} \times}{}$



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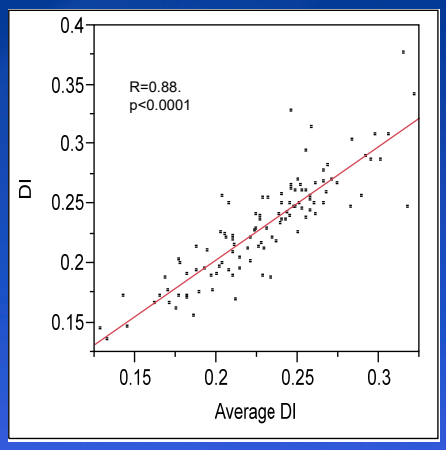
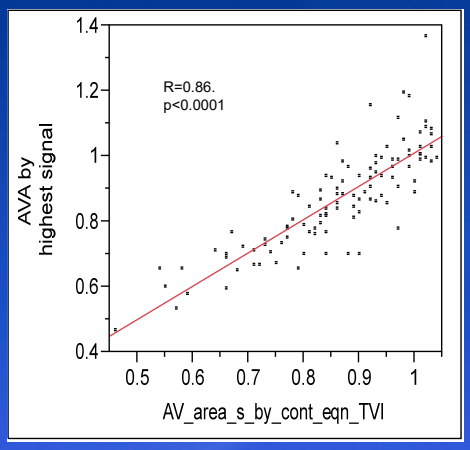
AVA and DI by averaged vs highest signals?





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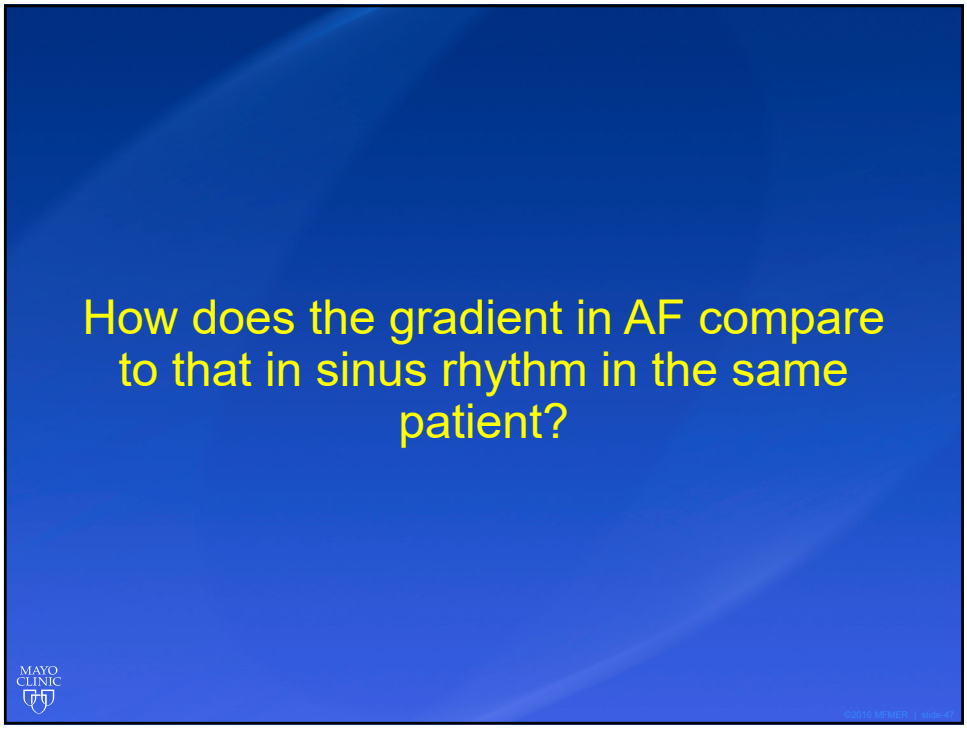
How does the gradient in AF compare to that in sinus rhythm in the same patient?
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DOI: 10.1111/echo.14020
ECHO ROUNDS Section Editors - Edmund Kenneth Kerut, MD and Michael R. McMullan, MD
WILEY Echocardiography
Aortic valve hemodynamics in atrial fibrillation: Should the highest Doppler signal be used to estimate severity of aortic stenosis?
Said Alsidawi MD[1] | Sana Khan MD[2] | Sorin V. Pislaru MD, PhD[2] | Vuyisile T. Nkomo MD, MPH[2]
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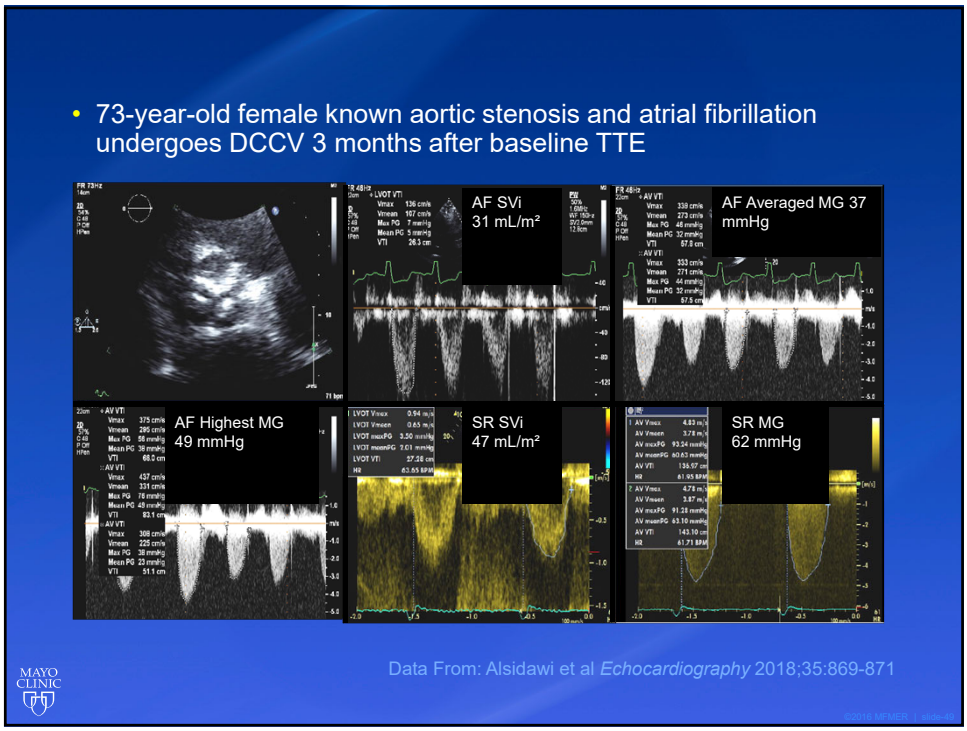
• 73-year-old female known aortic stenosis and atrial fibrillation undergoes DCCV 3 months after baseline TTE
AF SVi
31 mL/m²
AF Averaged MG 37
mmHg
AF Highest MG
49 mmHg
SR SVi
47 mL/m²
SR MG
62 mmHg
Data From: Alsidawi et al Echocardiography 2018;35:869-871

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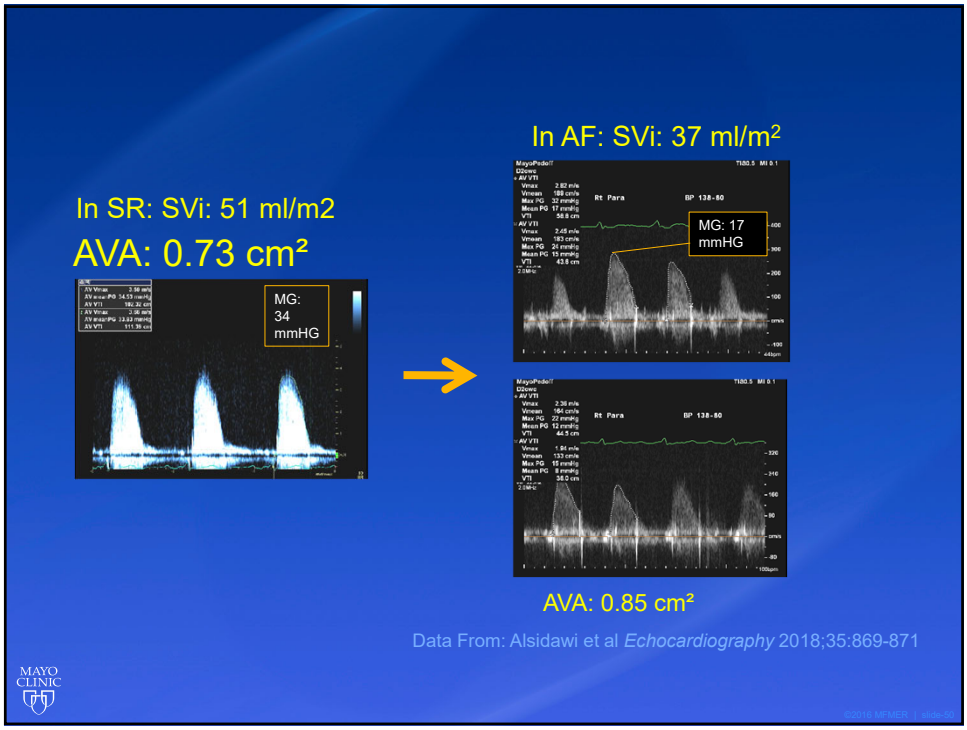
In SR: SVi: 51 ml/m2
AVA: 0.73 cm²
MG:
34
mmHG
In AF: SVi: 37 ml/m²
MG: 17
mmHG
AVA: 0.85 cm²
Data From: Alsidawi et al Echocardiography 2018;35:869-871

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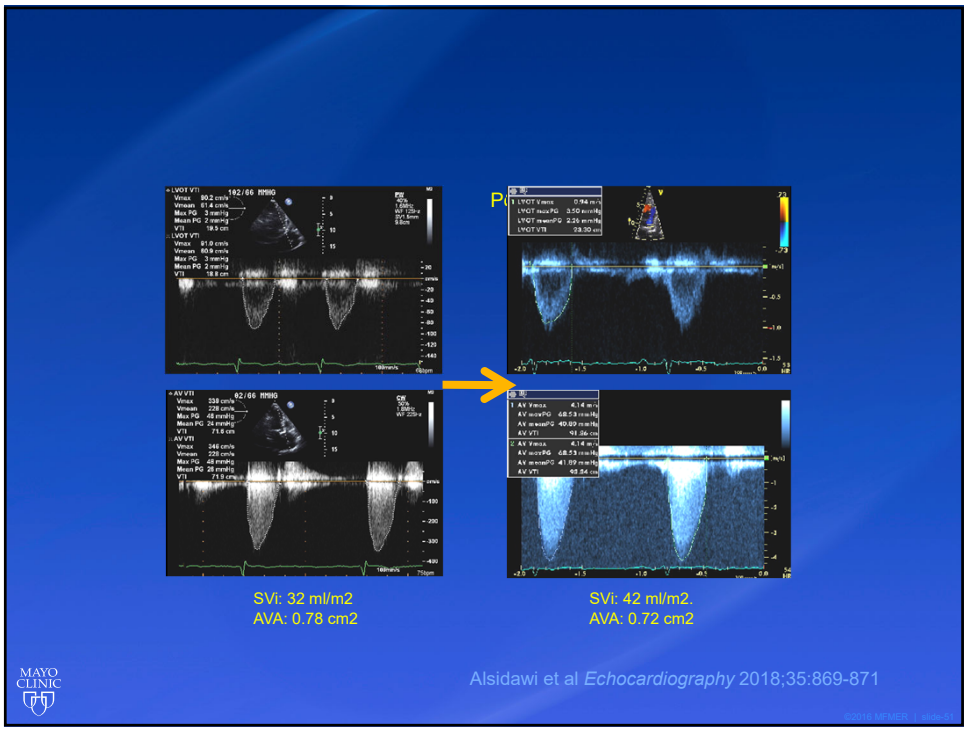
SVi: 32 ml/m2
AVA: 0.78 cm2
SVi: 42 ml/m2.
AVA: 0.72 cm2
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Alsidawi et al *Echocardiography* 2018;35:869-871

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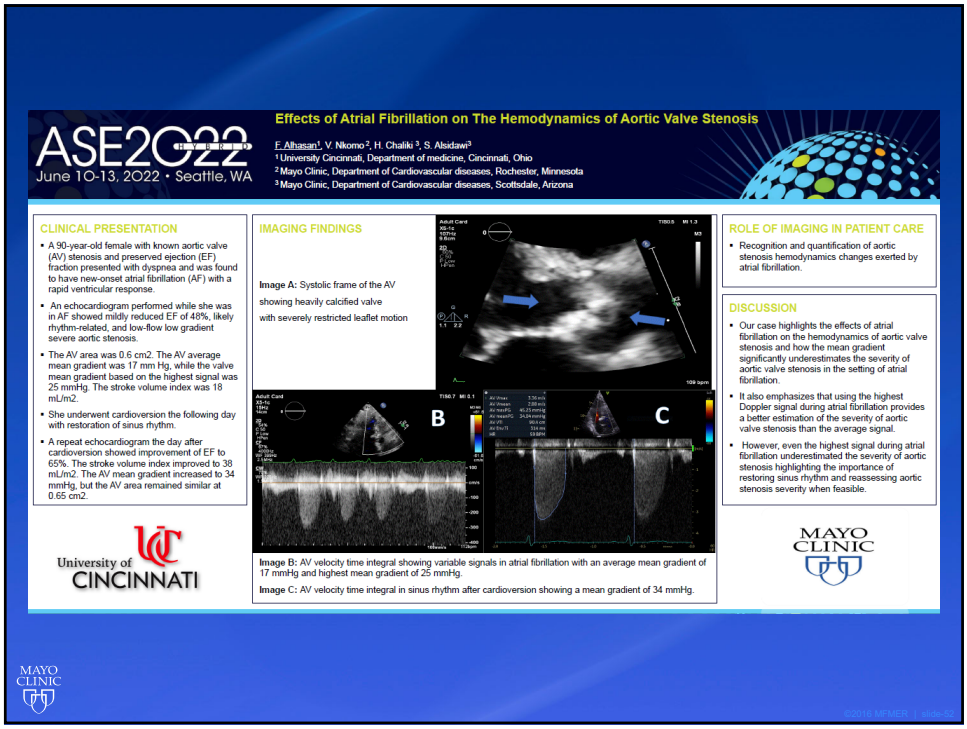
ASE2022
June 10-13, 2022 • Seattle, WA
Effects of Atrial Fibrillation on The Hemodynamics of Aortic Valve Stenosis
F. Alhasan[1], V. Nkomo[2], H. Chaliki[3], S. Alsidawi[3]
[1] University Cincinnati, Department of medicine, Cincinnati, Ohio
[2] Mayo Clinic, Department of Cardiovascular diseases, Rochester, Minnesota
[3] Mayo Clinic, Department of Cardiovascular diseases, Scottsdale, Arizona
CLINICAL PRESENTATION
• A 90-year-old female with known aortic valve (AV) stenosis and preserved ejection (EF) fraction presented with dyspnea and was found to have new-onset atrial fibrillation (AF) with a rapid ventricular response.
• An echocardiogram performed while she was in AF showed mildly reduced EF of 48%, likely rhythm-related, and low-flow low gradient severe aortic stenosis.
• The AV area was 0.6 cm2. The AV average mean gradient was 17 mm Hg, while the valve mean gradient based on the highest signal was 25 mmHg. The stroke volume index was 18 mL/m2.
• She underwent cardioversion the following day with restoration of sinus rhythm.
• A repeat echocardiogram the day after cardioversion showed improvement of EF to 65%. The stroke volume index improved to 38 mL/m2. The AV mean gradient increased to 34 mmHg, but the AV area remained similar at 0.65 cm2.
IMAGING FINDINGS
Image A: Systolic frame of the AV showing heavily calcified valve with severely restricted leaflet motion
B
C
Image B: AV velocity time integral showing variable signals in atrial fibrillation with an average mean gradient of 17 mmHg and highest mean gradient of 25 mmHg.
Image C: AV velocity time integral in sinus rhythm after cardioversion showing a mean gradient of 34 mmHg.
ROLE OF IMAGING IN PATIENT CARE
• Recognition and quantification of aortic stenosis hemodynamics changes exerted by atrial fibrillation.
DISCUSSION
• Our case highlights the effects of atrial fibrillation on the hemodynamics of aortic valve stenosis and how the mean gradient significantly underestimates the severity of aortic valve stenosis in the setting of atrial fibrillation.
• It also emphasizes that using the highest Doppler signal during atrial fibrillation provides a better estimation of the severity of aortic valve stenosis than the average signal.
• However, even the highest signal during atrial fibrillation underestimated the severity of aortic stenosis highlighting the importance of restoring sinus rhythm and reassessing aortic stenosis severity when feasible.
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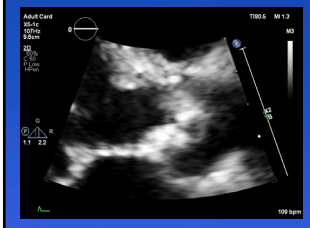
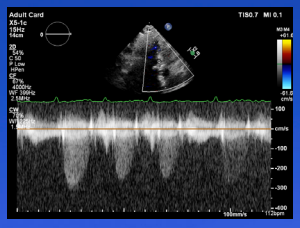
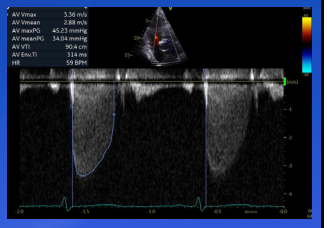
- 90-year-old female with known aortic valve stenosis.
- She presented to the hospital with shortness of breath and was found to be in atrial fibrillation with rapid ventricular response.
- Echo 1 in AF: SVI 21 ml/m2. Avg. MG: 17 mmHg. Peak MG: 23 mmHg. AVA: 0.7 cm2
- Echo 2 in SR just 2 days after initial echo: SVI 37 ml/m2. MG: 34 mmHg. AVA: 0.7 cm2.

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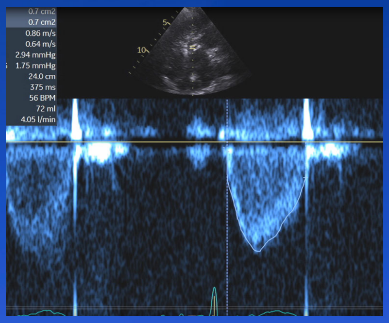
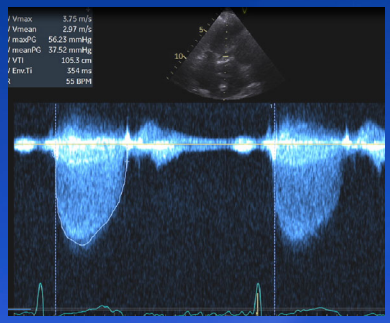
Echo 3 a month later: SVI now up to 42 ml/m2 and MG up to 38 mmHg. AVA is unchanged.

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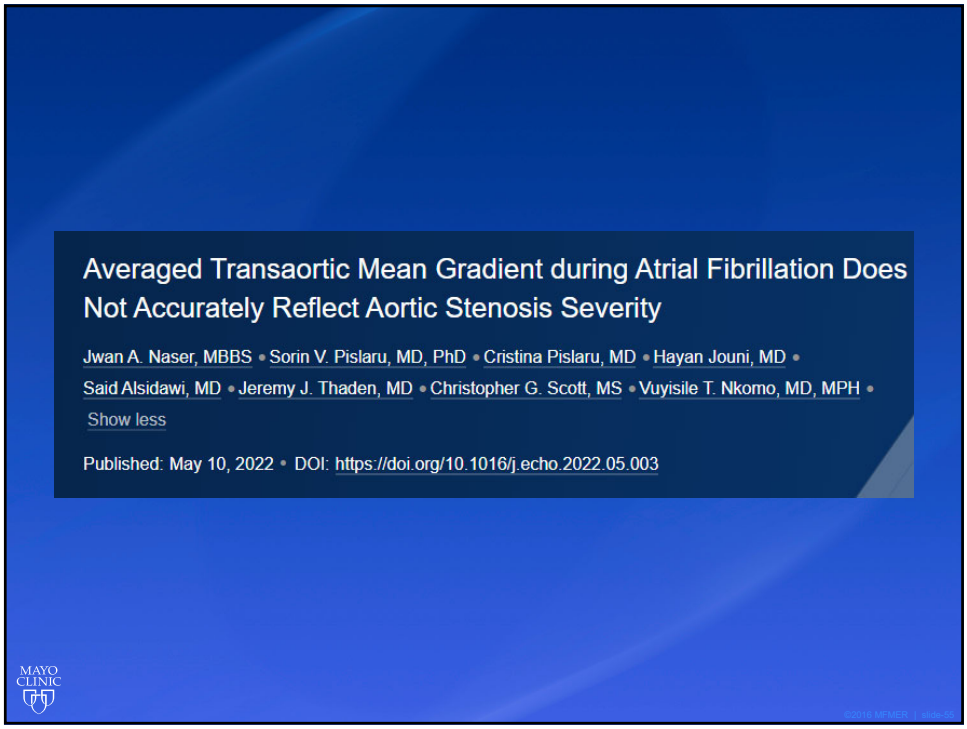
Averaged Transaortic Mean Gradient during Atrial Fibrillation Does Not Accurately Reflect Aortic Stenosis Severity
Jwan A. Naser, MBBS • Sorin V. Pislaru, MD, PhD • Cristina Pislaru, MD • Hayan Jouni, MD • Said Alsidawi, MD • Jeremy J. Thaden, MD • Christopher G. Scott, MS • Vuyisile T. Nkomo, MD, MPH •
Show less
Published: May 10, 2022 • DOI: https://doi.org/10.1016/j.echo.2022.05.003
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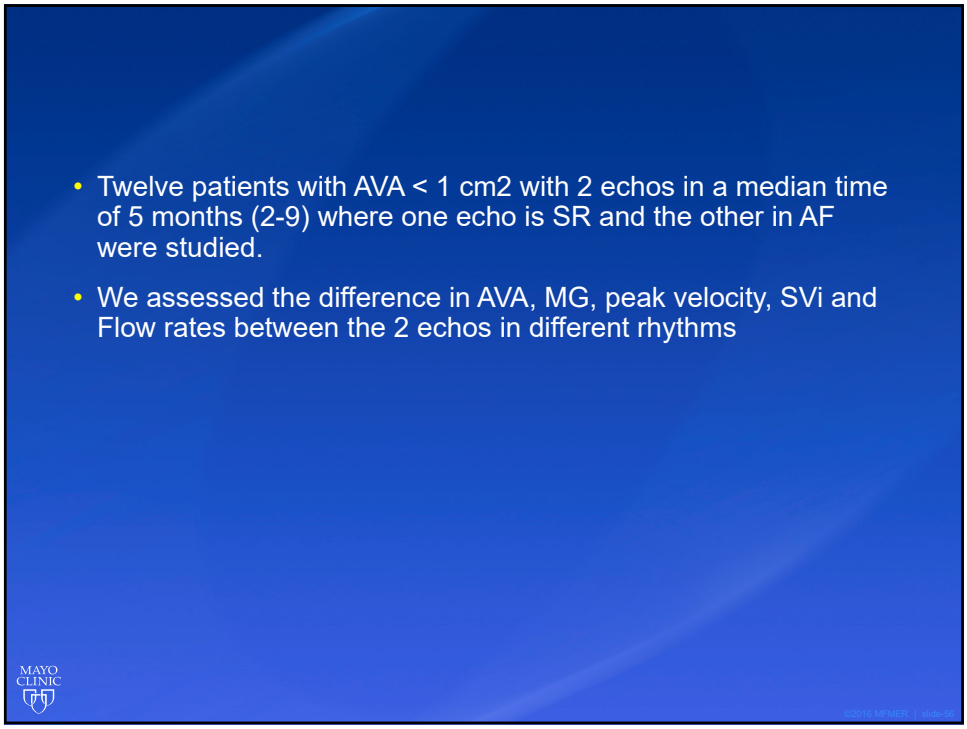
• Twelve patients with AVA < 1 cm2 with 2 echos in a median time of 5 months (2-9) where one echo is SR and the other in AF were studied.
• We assessed the difference in AVA, MG, peak velocity, SVi and Flow rates between the 2 echos in different rhythms
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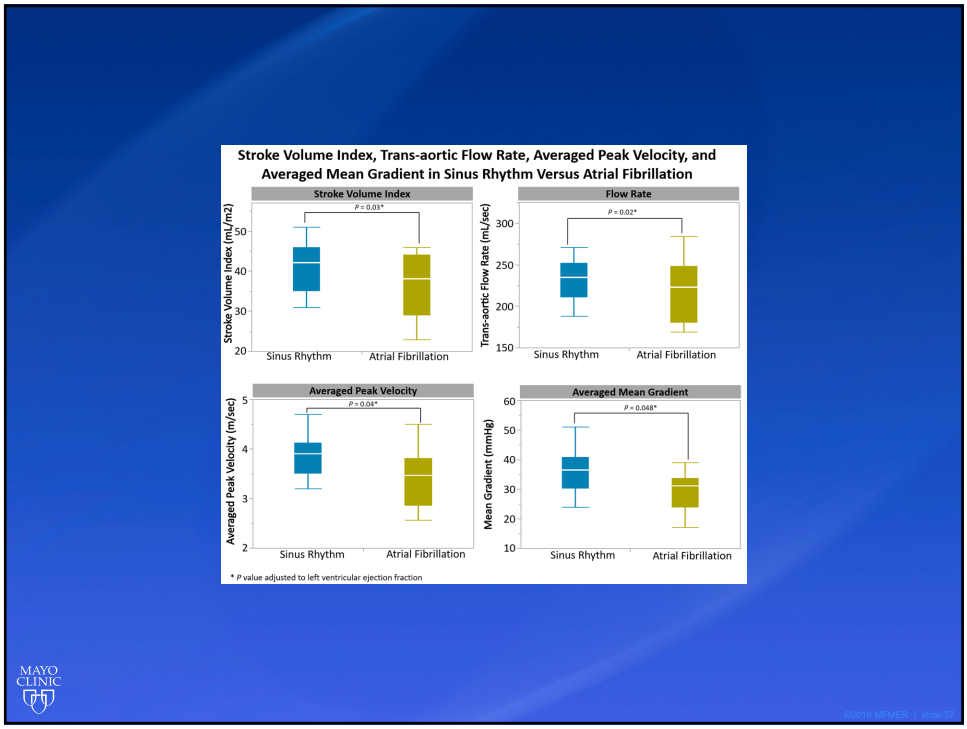
Stroke Volume Index, Trans-aortic Flow Rate, Averaged Peak Velocity, and Averaged Mean Gradient in Sinus Rhythm Versus Atrial Fibrillation
Stroke Volume Index
Stroke Volume Index (mL/m2)
P = 0.03*
Sinus Rhythm
Atrial Fibrillation
Flow Rate
Trans-aortic Flow Rate (mL/sec)
P = 0.02*
Averaged Peak Velocity
Averaged Peak Velocity (m/sec)
P = 0.04*
Averaged Mean Gradient
Mean Gradient (mmHg)
P = 0.048*
* P value adjusted to left ventricular ejection fraction
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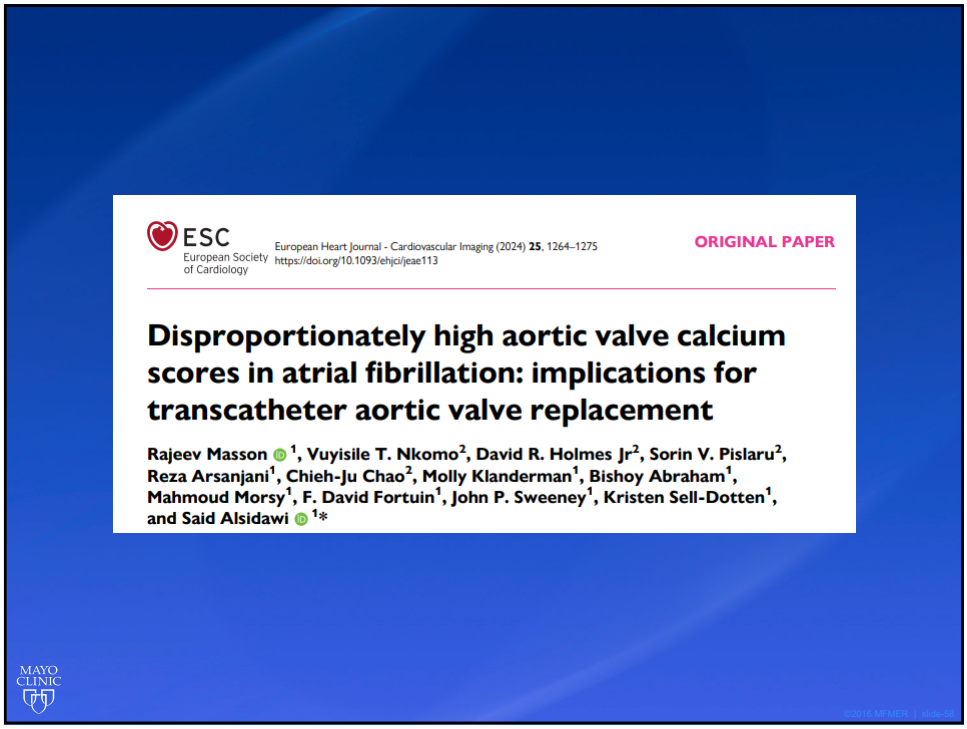
ESC
European Society of Cardiology
European Heart Journal - Cardiovascular Imaging (2024) 25, 1264–1275
https://doi.org/10.1093/ehjci/jeae113
ORIGINAL PAPER
Disproportionately high aortic valve calcium scores in atrial fibrillation: implications for transcatheter aortic valve replacement
Rajeev Masson [1], Vuyisile T. Nkomo[2], David R. Holmes Jr[2], Sorin V. Pislaru[2], Reza Arsanjani[1], Chieh-Ju Chao[2], Molly Klanderman[1], Bishoy Abraham[1], Mahmoud Morsy[1], F. David Fortuin[1], John P. Sweeney[1], Kristen Sell-Dotten[1], and Said Alsidawi [1]*
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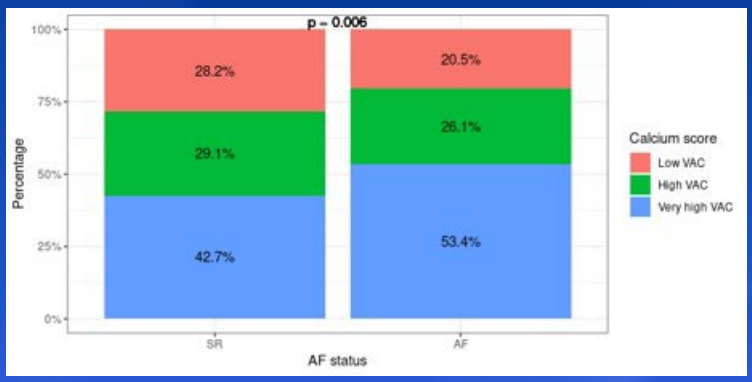
Table 1: Demographics and clinical characteristics by atrial fibrillation status				
	SR (N=464)	AF (N=356)	Total (N=820)	P value
Age at procedure	80.5 (8.6)	82.2 (7.5)	81.3 (8.2)	**0.003**



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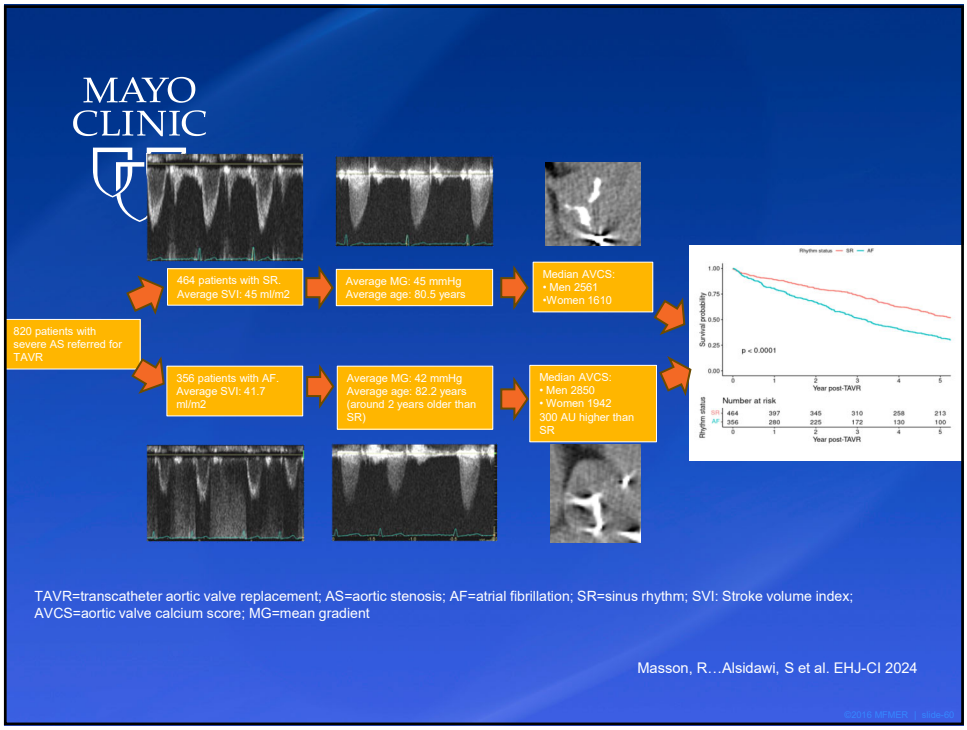

TAVR=transcatheter aortic valve replacement; AS=aortic stenosis; AF=atrial fibrillation; SR=sinus rhythm; SVI: Stroke volume index; AVCS=aortic valve calcium score; MG=mean gradient

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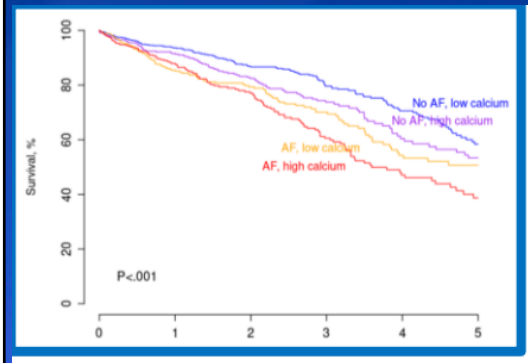

490 deaths occurred over a median follow-up of 2.25 (IQR: 1.03 - 4.00) years.

Patients with AF and high AVCS (>2428 AU) had the lowest 5-year survival (38.5%).

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Characteristic	2-year prior N = 136[1]	TAVI N = 136[1]	P-value[2]
EF%	61 (55, 66)	57 (46, 64)	<0.001
E/ARatio	1.08 (0.80, 1.33)	1.25 (0.80, 2.00)	<0.001
E/e'Ratio(medial)	20 (15, 25)	18 (0, 27)	<0.001
LAVI	46 (38, 57)	52 (43, 63)	0.006
MPG	30 (21, 38)	41 (32, 48)	<0.001
Peak velocity	3.50 (3.00, 4.00)	4.10 (3.70, 4.50)	<0.001
AVA (TVI)	1.08 (0.87, 1.28)	0.84 (0.68, 0.94)	<0.001
AVA Index (Velocity)	0.55 (0.47, 0.65)	0.45 (0.38, 0.51)	<0.001
AVA Index (TVI)	0.53 (0.46, 0.65)	0.43 (0.36, 0.49)	<0.001
LVSVI	45 (39, 52)	42 (36, 50)	0.016
RV function (TAPSE)	17 (14, 21)	18 (13, 21)	0.319
Moderate or severe MR	24 (17.6%)	49 (36%)	<0.001
Moderate or severe TR	31 (22.7%)	49 (36%)	<0.001

Under review

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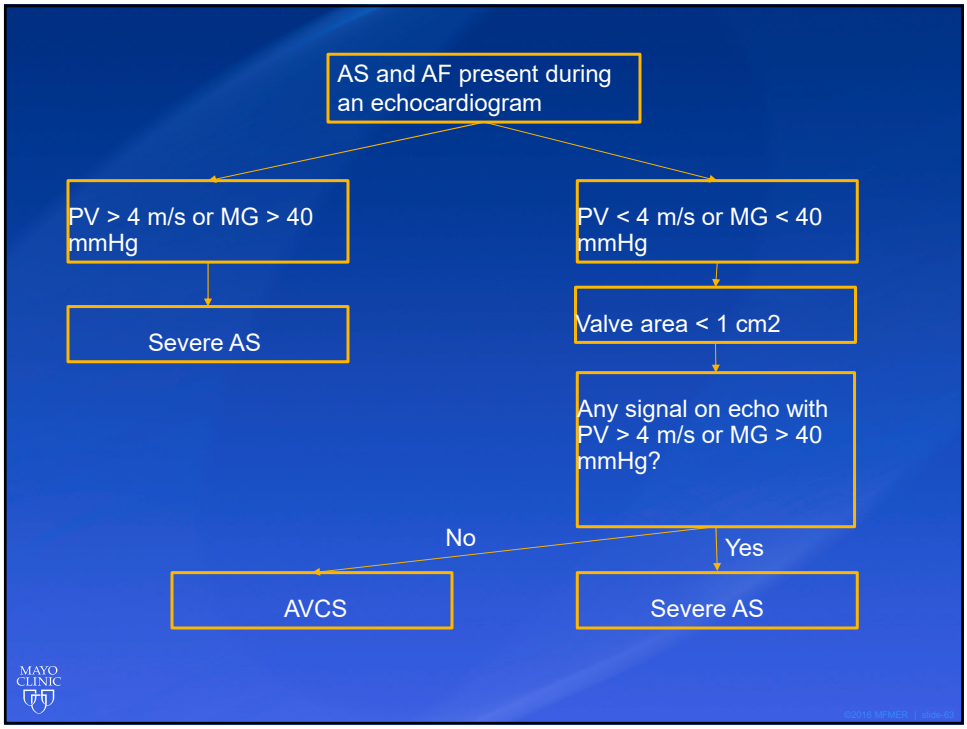

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Conclusion:

- Averaging under-estimates the severity of aortic valve stenosis.
- We are under-referring patients with AS and AF by averaging their signals.
- Think about severe AS when faced with LGAS in the setting of AF.
- The highest signal should be used to grade AS in these patients.
- AVCS is a helpful measure to confirm severity of aortic stenosis in certain cases.

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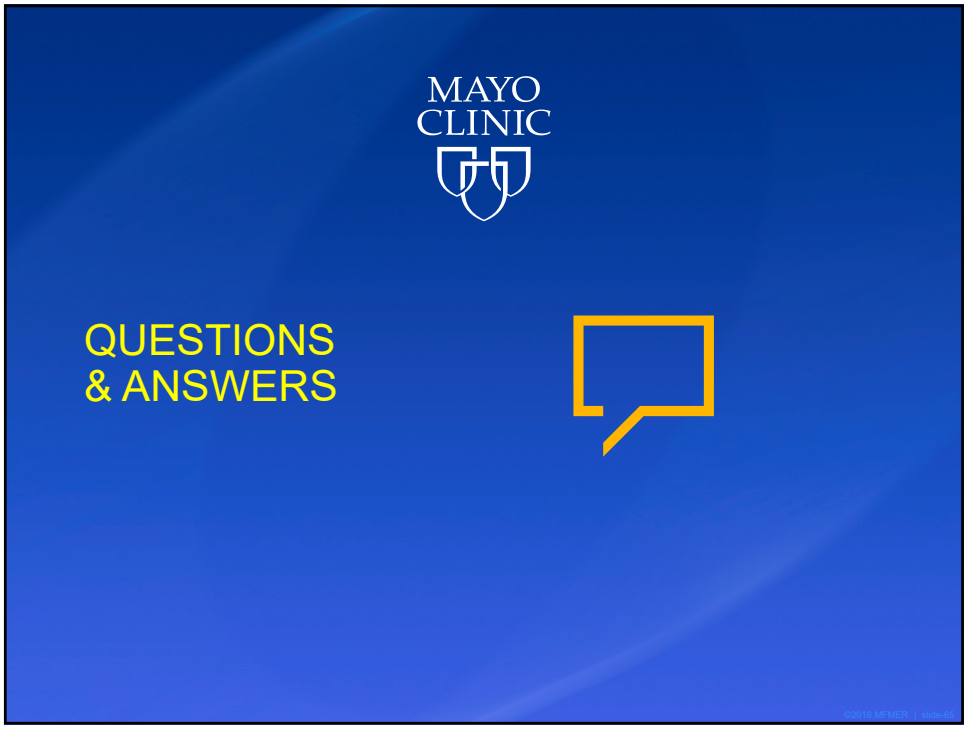

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