Aortic Stenosis Background and Breakthroughs in Treatment: TAVR Update

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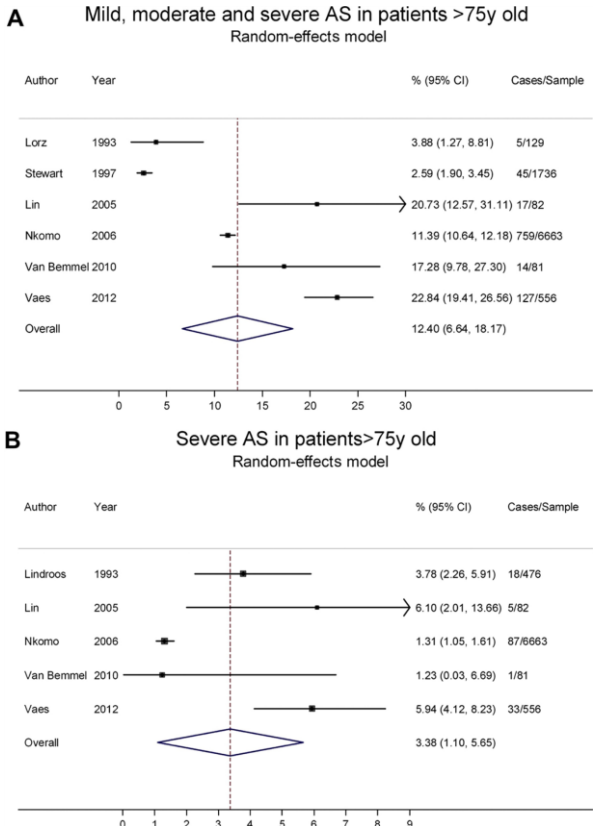
Disclosures for Howard J Broder MD

- As of 2017 I speak and proctor for
  - Abiomed
  - Medtronic

Aortic Stenosis- Overview

- Aortic Stenosis is a common finding in the elderly, and is associated with significant morbidity and mortality.
- The presenting symptoms are often referred to as the triad of symptoms-
  - Angina/ Dyspnea/ Syncope
- These are often the presenting symptoms of an inpatient hospitalization. Additionally, the finding of Aortic Stenosis may be a secondary or contributing factor to another reason for hospitalization.
- Once identified, expeditious evaluation and treatment is recommended.

Aortic Stenosis- Prevalence



- Prevalence of 12.4% in the >75 y/o population corresponds to 2.7 million people in North America.
- 540,000 are severe/ symptomatic.
- 40% do not get SAVR.
- With expected increases in life expectancy, this will increase to 800,000 by 2025 and 1.4M by 2050.

From: Aortic Stenosis in the Elderly: Disease Prevalence and Number of Candidates for Transcatheter Aortic Valve Replacement: A Meta-Analysis and Modeling Study

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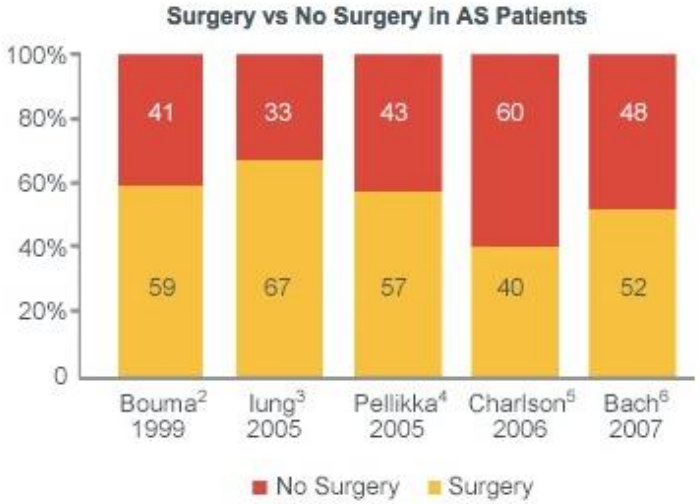
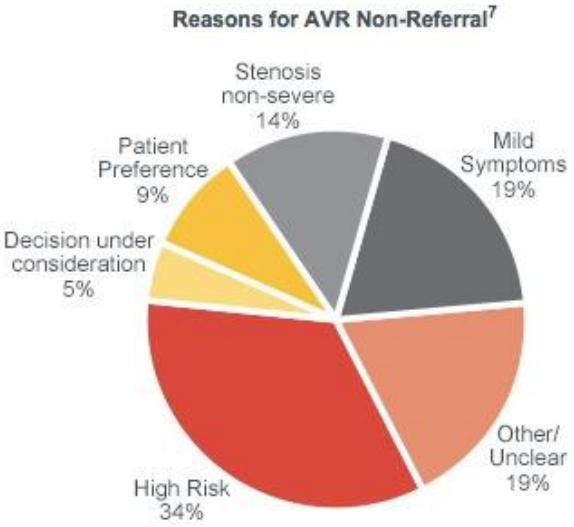
Aortic Stenosis- nonreferral for AVR



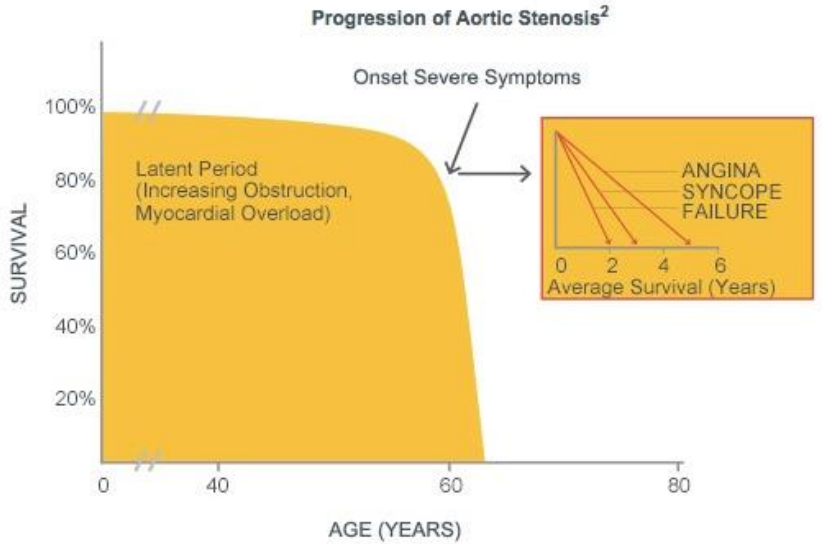
Guidelines are not consistently followed. In actual practice, more than one third of patients eligible for AVR are not referred for evaluation. As the chart illustrates, five different surveys identified 33% to 60% of patients not referred for surgery. Additionally, the Euro Heart Survey of 5000 patients from 92 centers in 25 European countries determined that 32.3% of patients over the age of 75 were denied surgery.[1]

Aortic Stenosis- reasons for nonreferral



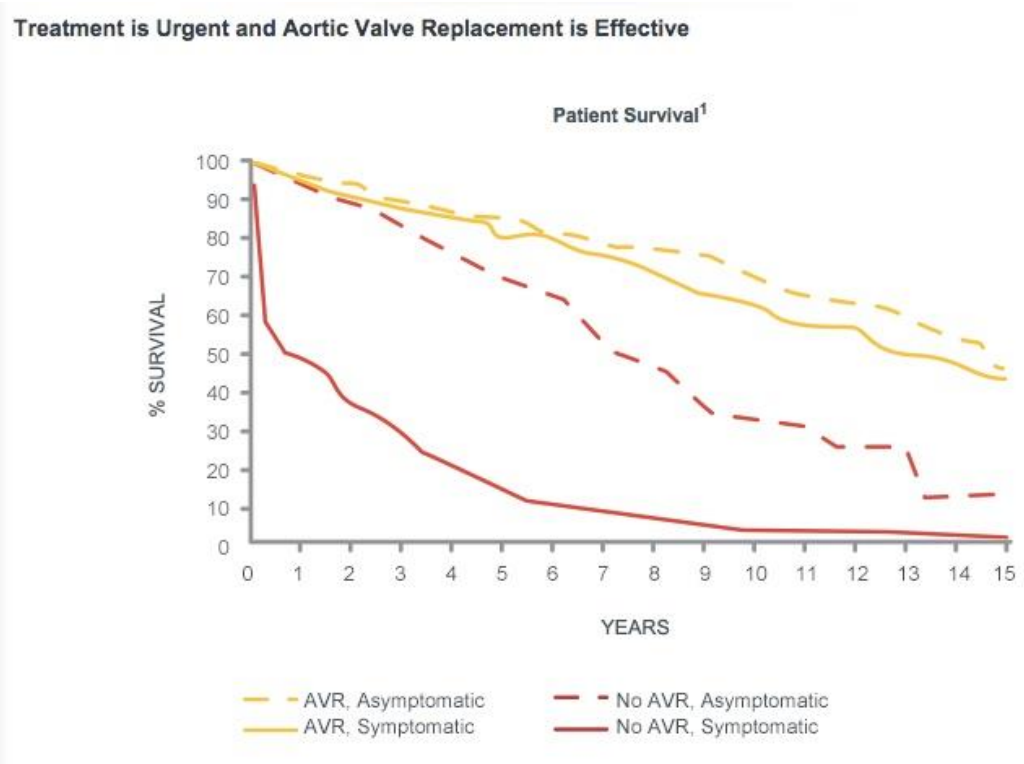
Treatment decisions for older patients with severe AS are challenging due to comorbidity; they have a higher operative risk and have reduced life expectancy. In addition, their risk is increased by comorbidities such as heart disease and other conditions that are often present in this age group.[8]

Natural History of Symptomatic AS



Valvular aortic stenosis is progressive and life-threatening. Once symptoms appear, untreated patients have a poor prognosis; they will experience worsening symptoms, eventually leading to death. After the onset of symptoms, average survival is 50% at two years and 20% at five years.[2]

Treatment of AS is effective



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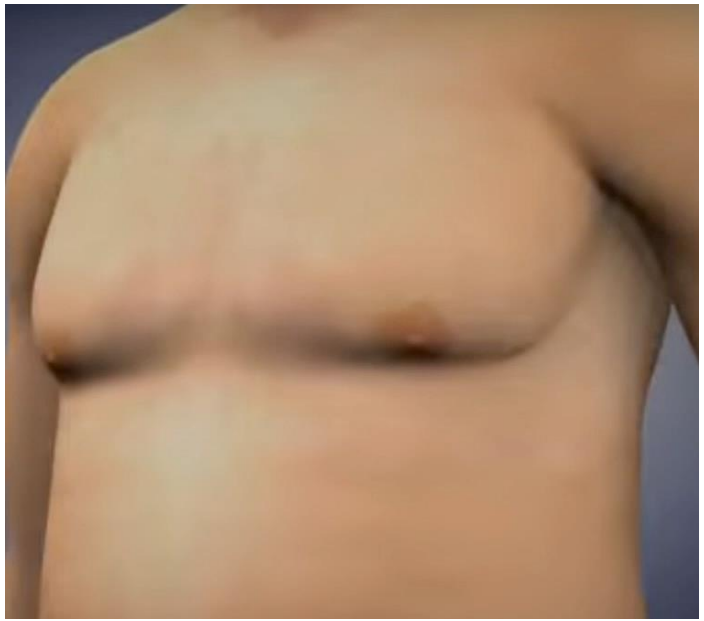
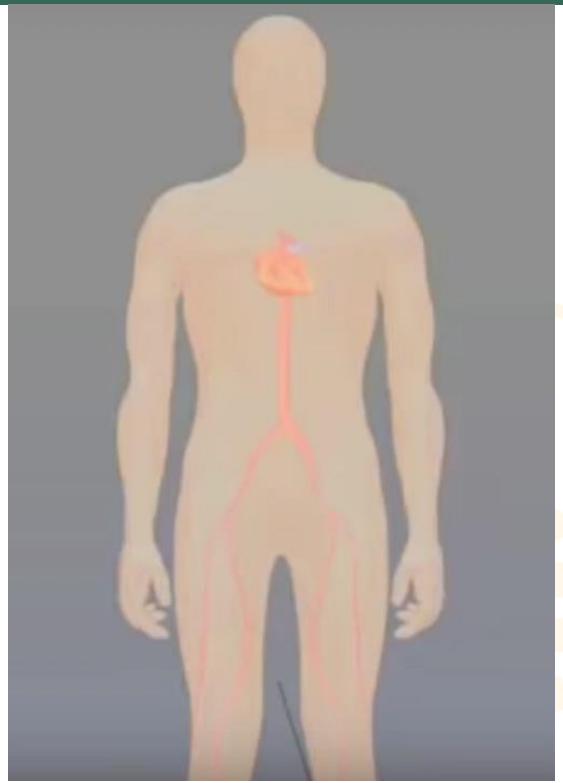
TAVR Genesis

- The first TAVR in man was performed in Rouen France in 2002 by Alain Cribier (Trained at Cedars Sinai)
- The first cases were actually done with a transseptal approach before the devices were modified for a retrograde aortic approach
- Cribier was instrumental in devoloping the Balloon Expandable Valves
- Self-Exanding Valves were developed contemporaneously
- To date worldwide there have been >200,000 TAVR implants

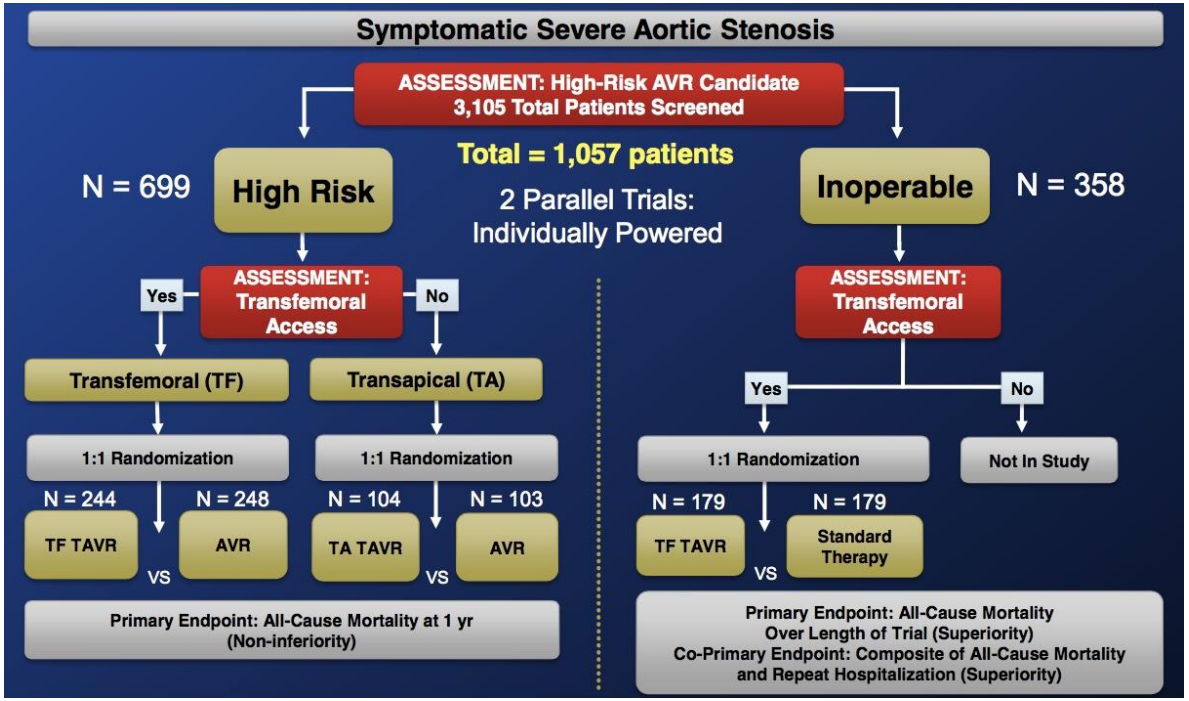
TAVR Genesis- Balloon Expandable vs Self Expanding:



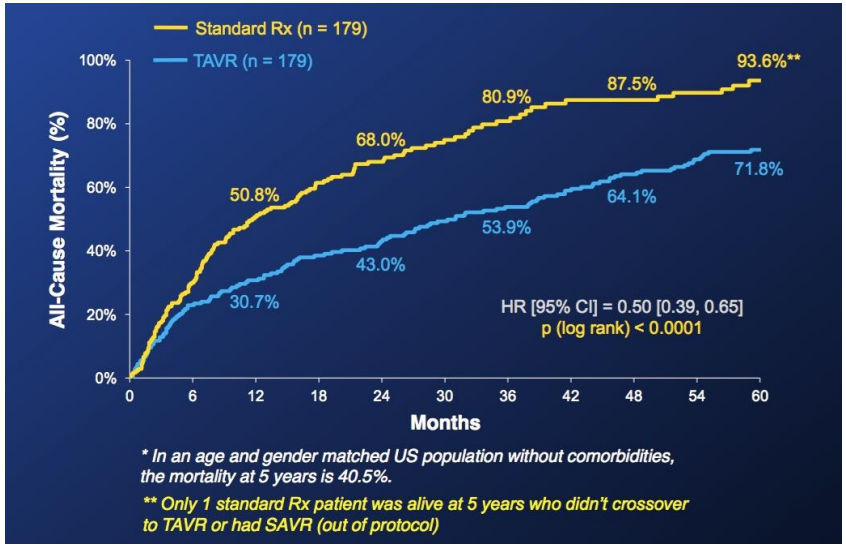


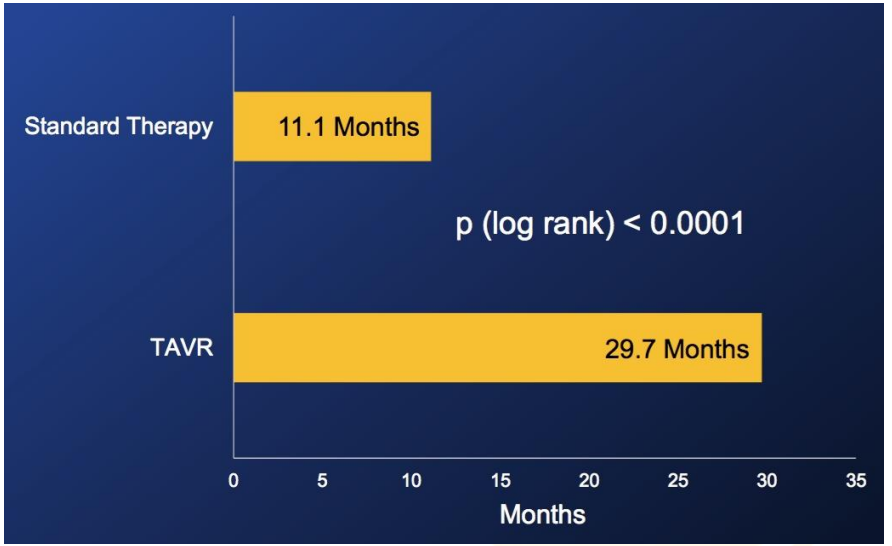
TAVR- Building a Body of Evidence: Partner Trial

- The Partner Trial was the first RCT designed to establish the safety and efficacy of TAVR in comparison to Standard (Med Rx) and SAVR.
- Initiated in 2007
- Divided into two parts (Inoperable A, and High Surgical Risk B)

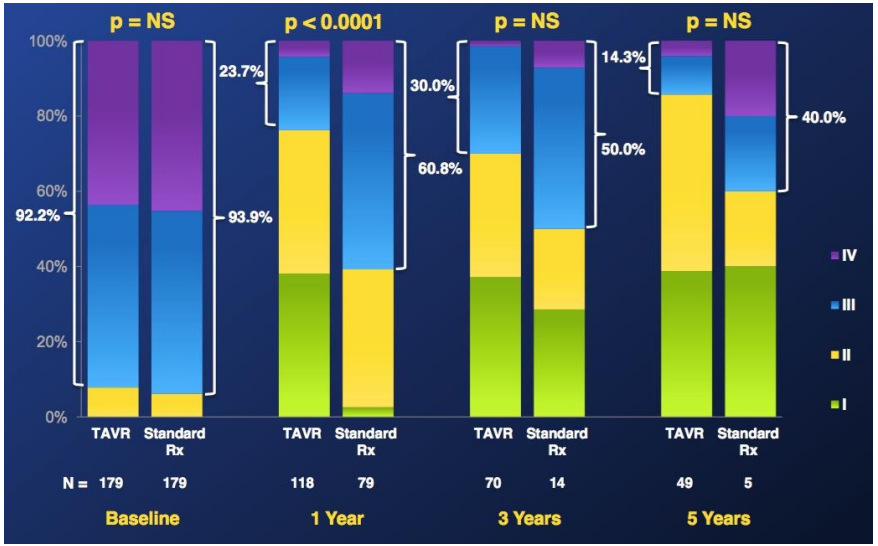


Partner A results: Inoperable Patients TAVR vs Med Rx





NYHA Class and Valve Performance



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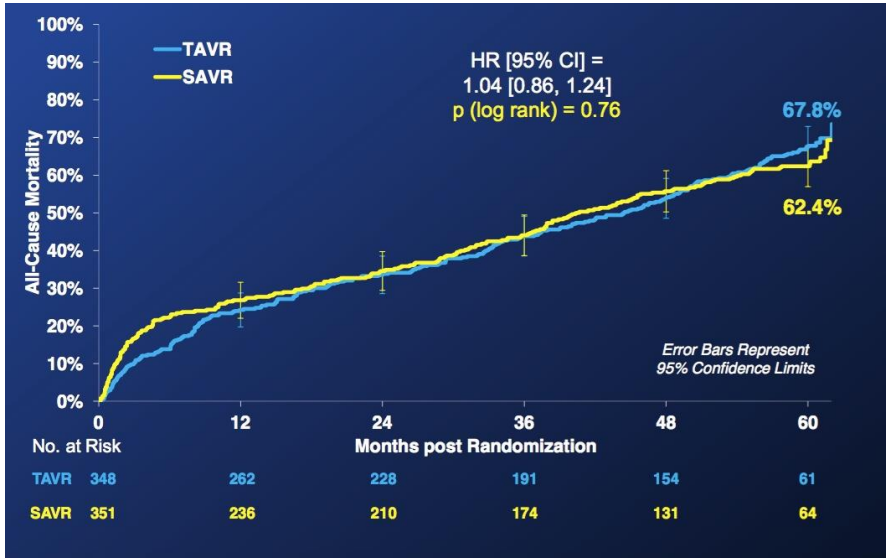
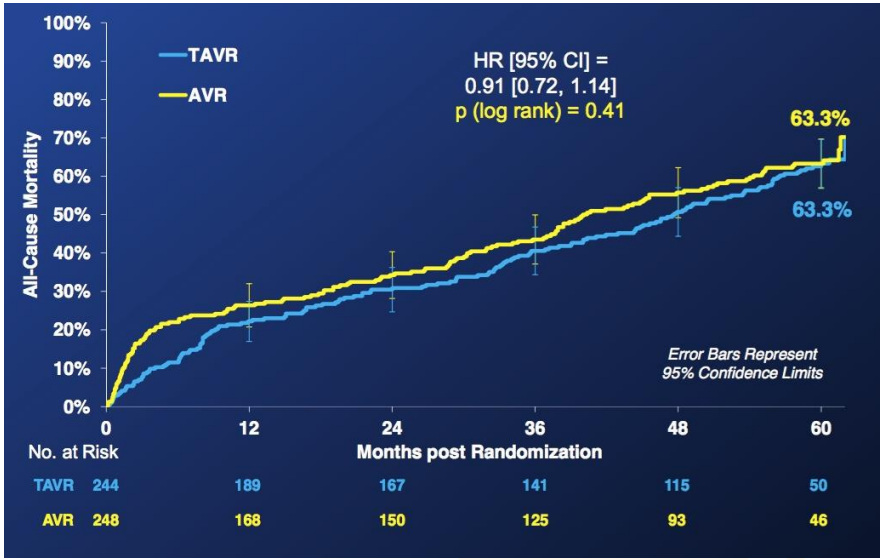
Partner B: High Risk Patients



All Patients (TF and TA)



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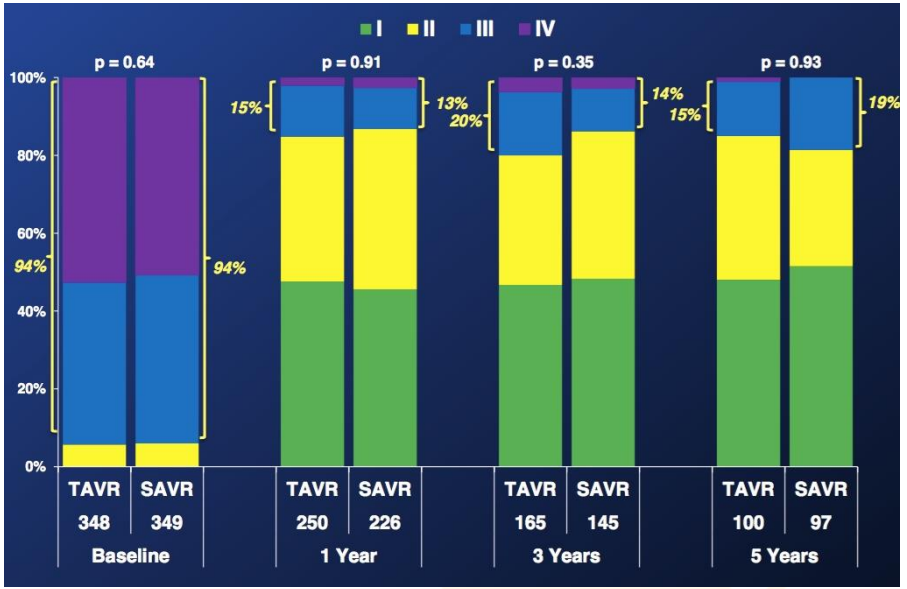
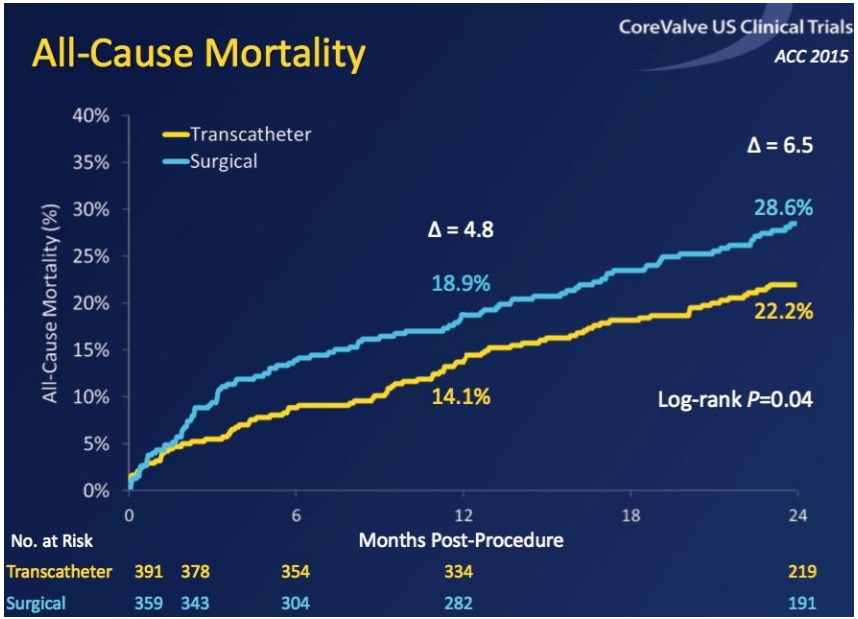
Partner B: High Risk Patients

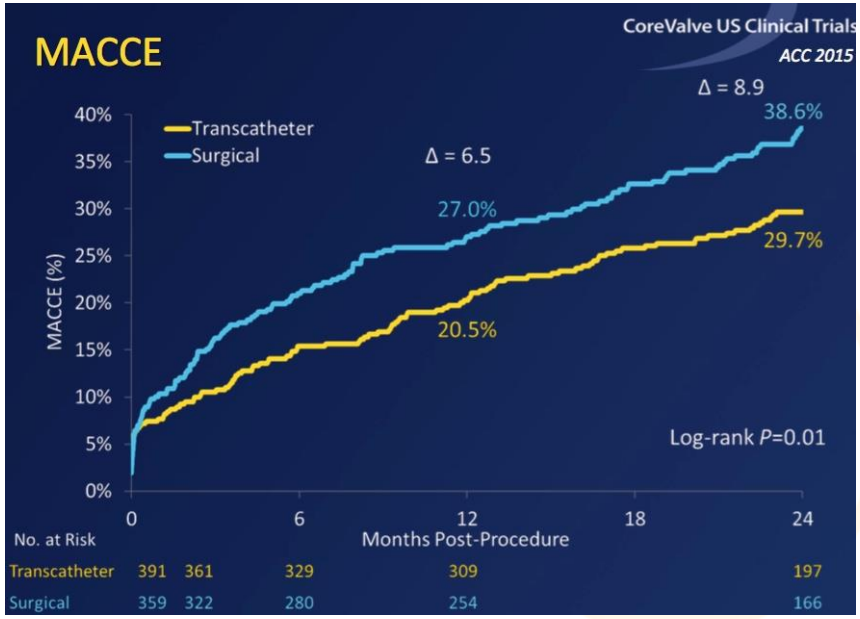


TAVR- Building a Body of Evidence- CoreValve Pivotal

- CoreValve was primarily a European Valve with CE Mark.
- The US Pivotal Trial started later than Partner.
- Randomization to Med Rx in Extreme Risk was no longer thought to be ethical.

CoreValve Pivotal Trial (TAVR vs SAVR)





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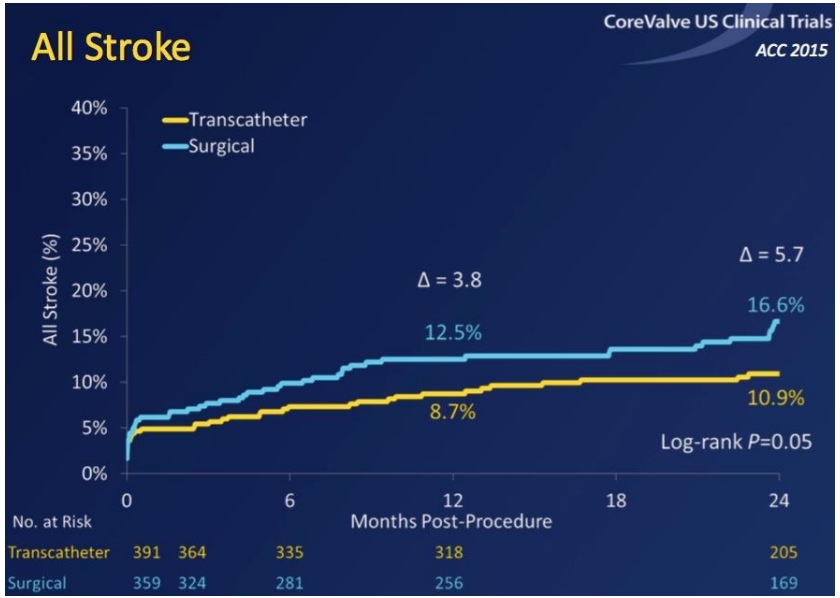
CoreValve Pivotal Trial

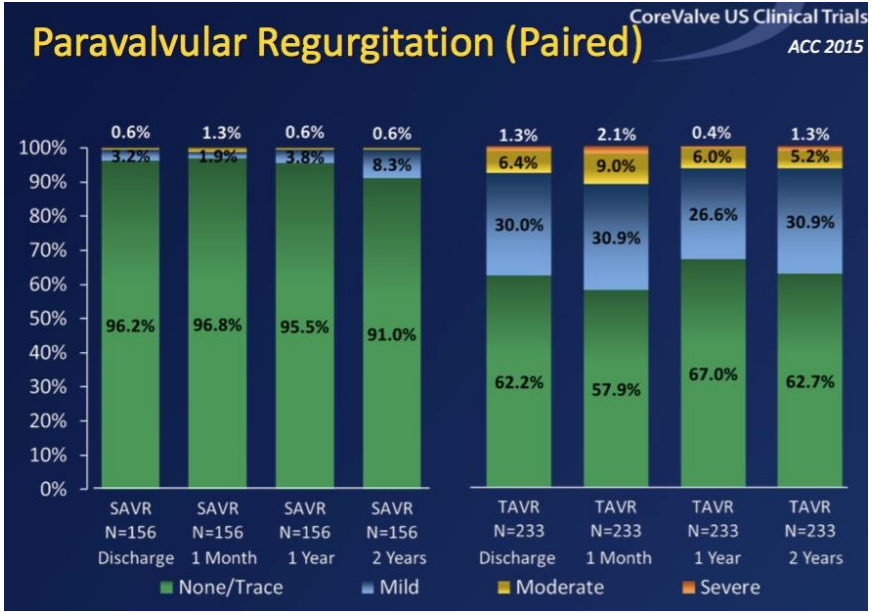


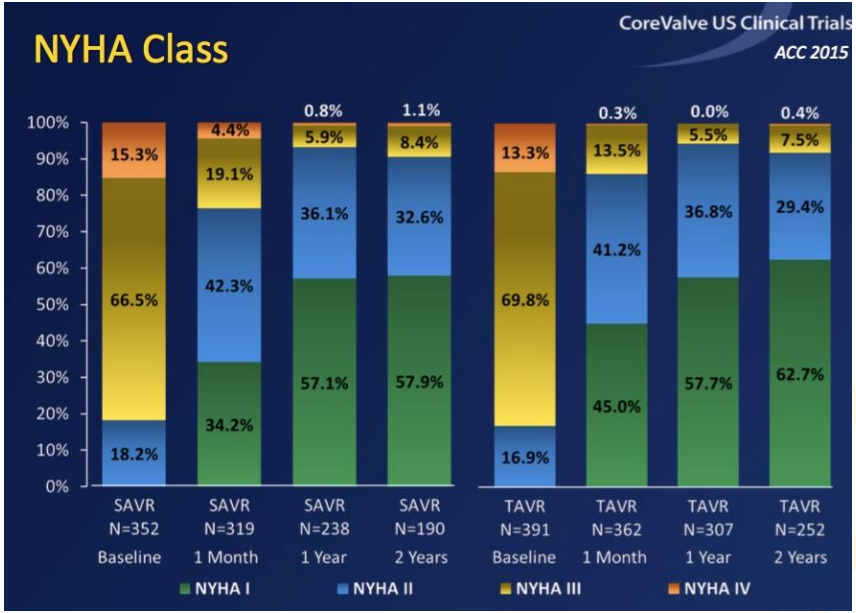
Other Clinical Endpoints

CoreValve US Clinical Trials
ACC 2015

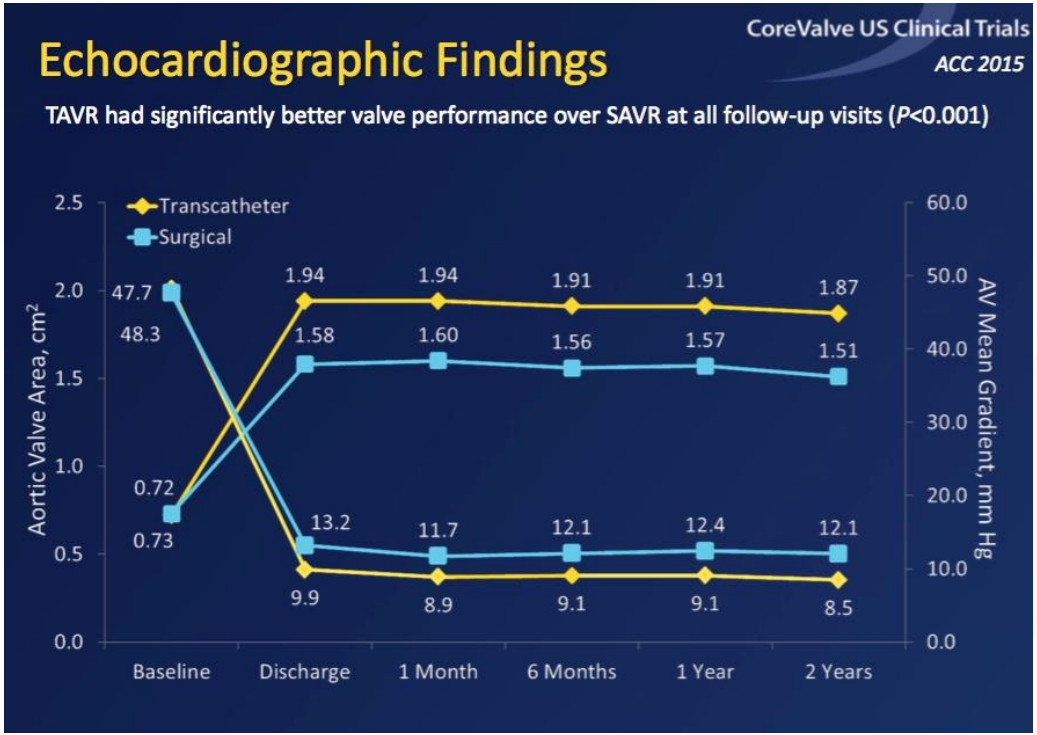
Events*	1 Month			1 Year			2 Years		
	TAVR	SAVR	*P*	TAVR	SAVR	*P*	TAVR	SAVR	*P*
Vascular complications (major)	6.2	1.7	0.002	6.4	2.0	0.003	7.1	2.0	0.001
Pacemaker implant	20.0	7.1	<0.001	22.5	11.6	<0.001	25.8	12.8	<0.001
Bleeding (life threatening or disabling)	13.6	35.1	<0.001	16.5	38.4	<0.001	18.1	39.6	<0.001
New onset or worsening atrial fibrillation	11.7	31.0	<0.001	16.4	33.2	<0.001	19.5	34.9	<0.001
Acute kidney injury	6.2	15.1	<0.001	6.2	15.1	<0.001	6.2	15.1	<0.001

CoreValve Pivotal Trial





CoreValve Pivotal Trial



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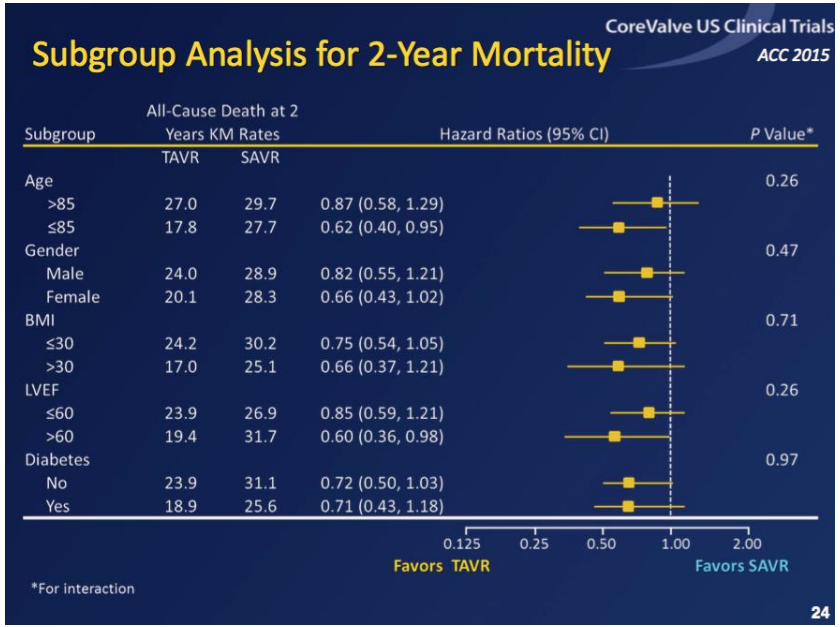
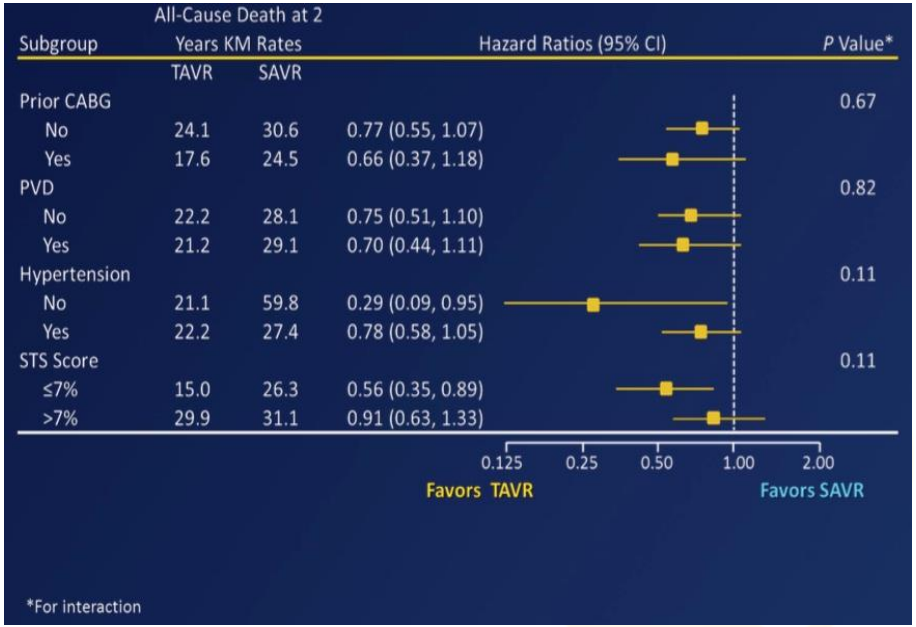
CoreValve Pivotal Trial

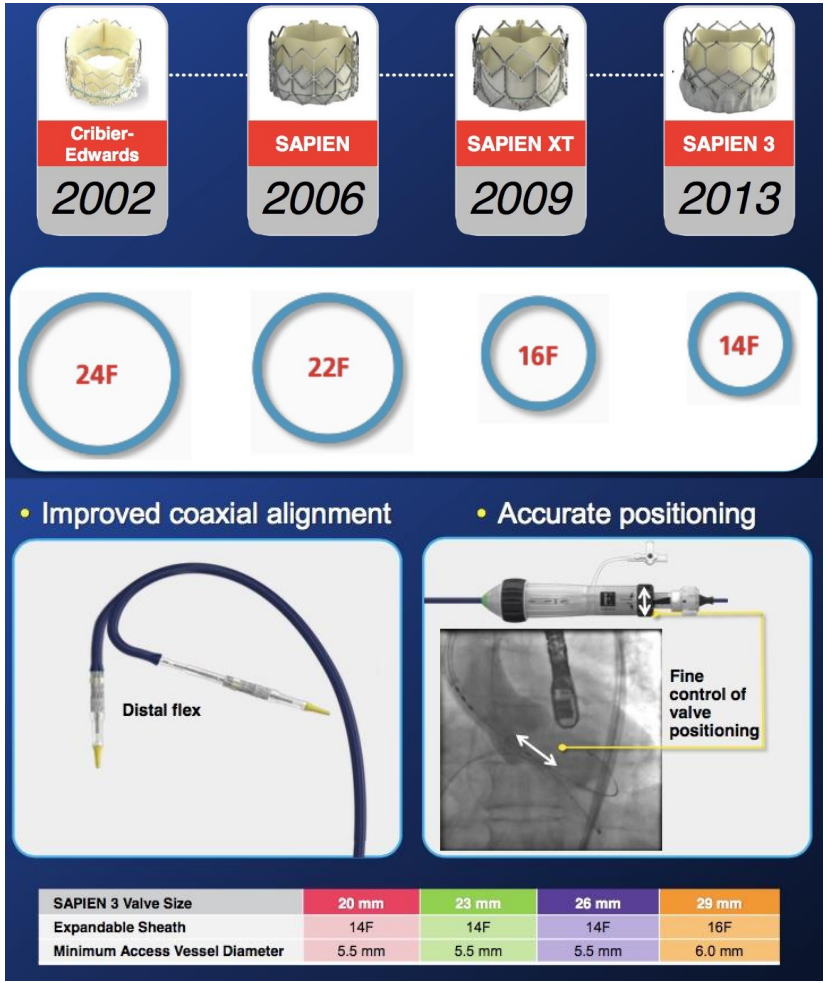




And now the bad news for SAVR…

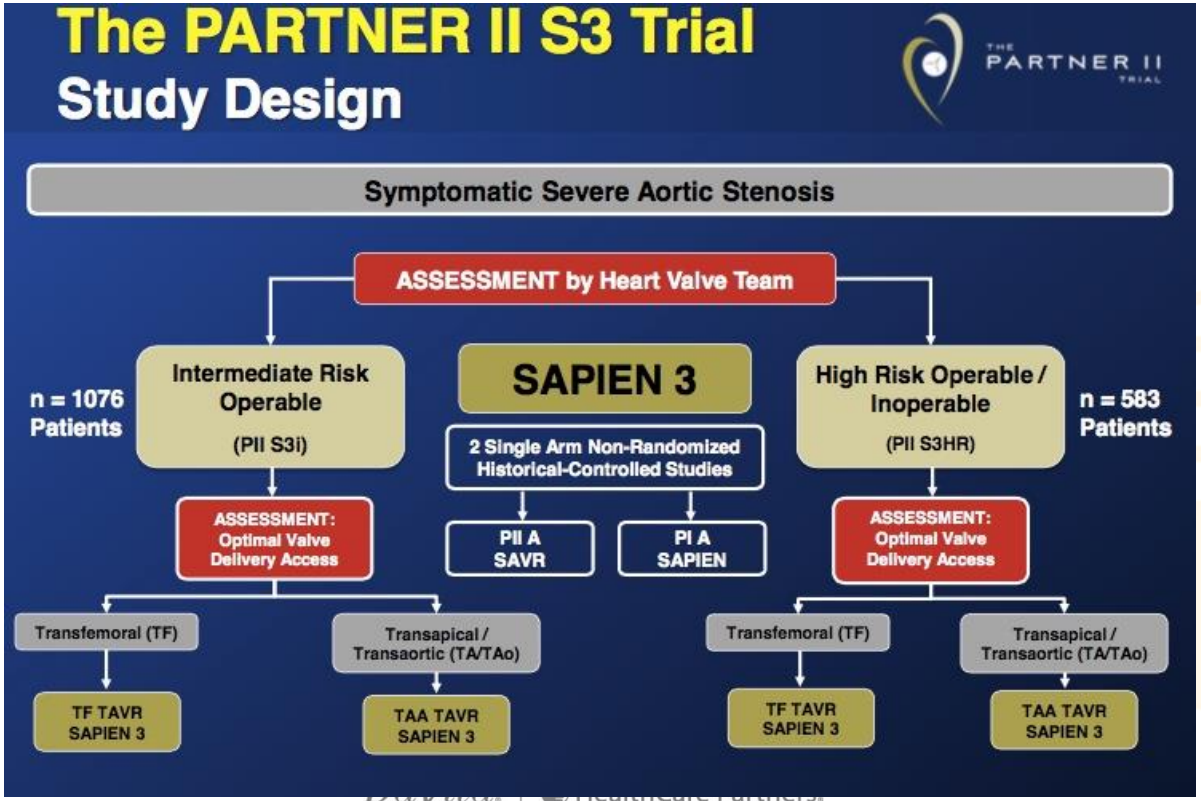
TAVR- State of the Art (S3)

- TAVR devices have become smaller and more precise, allowing for better, more reliable and reproducible deployments, and reduced vascular complications.
- Notable on the Sapien 3 is the smaller sheath size (Expandable E-Sheath).
- Distal flexing of the catheter can allow for a more coaxial deployment.
- Fine tuning adjustments can now be made via a dial on the delivery catheter allowing for millimeter corrections.
- Additionally a “skirt” is used to reduce paravalvular leak.

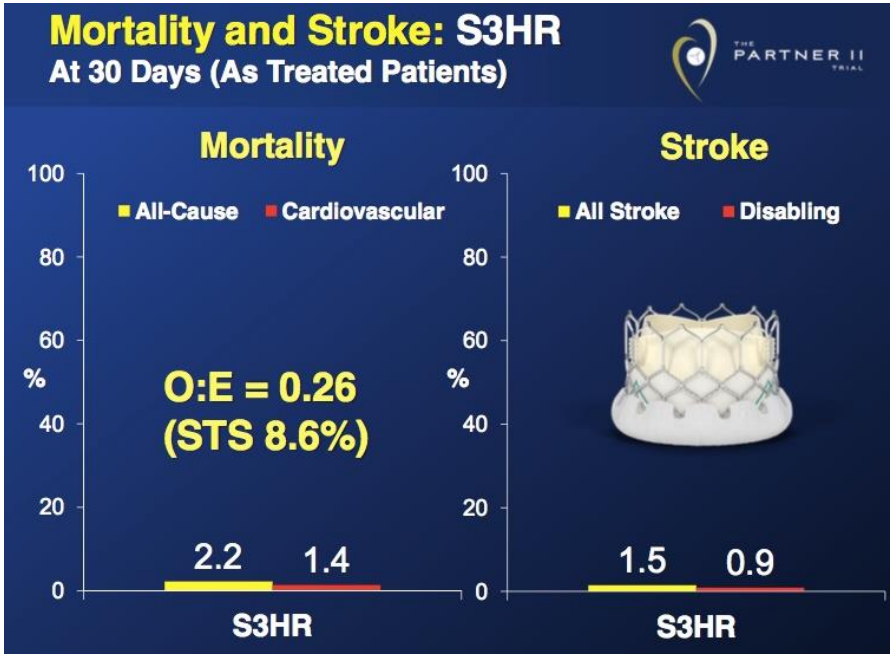


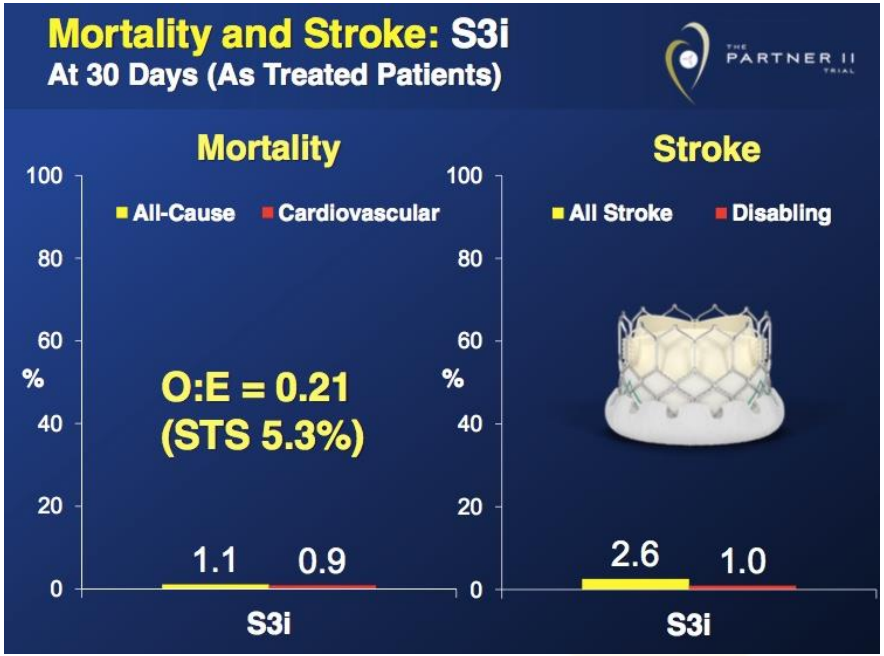
SAPIEN 3 Valve Size	20 mm	23 mm	26 mm	29 mm
Expandable Sheath	14F	14F	14F	16F
Minimum Access Vessel Diameter	5.5 mm	5.5 mm	5.5 mm	6.0 mm

TAVR- State of the Art (S3)

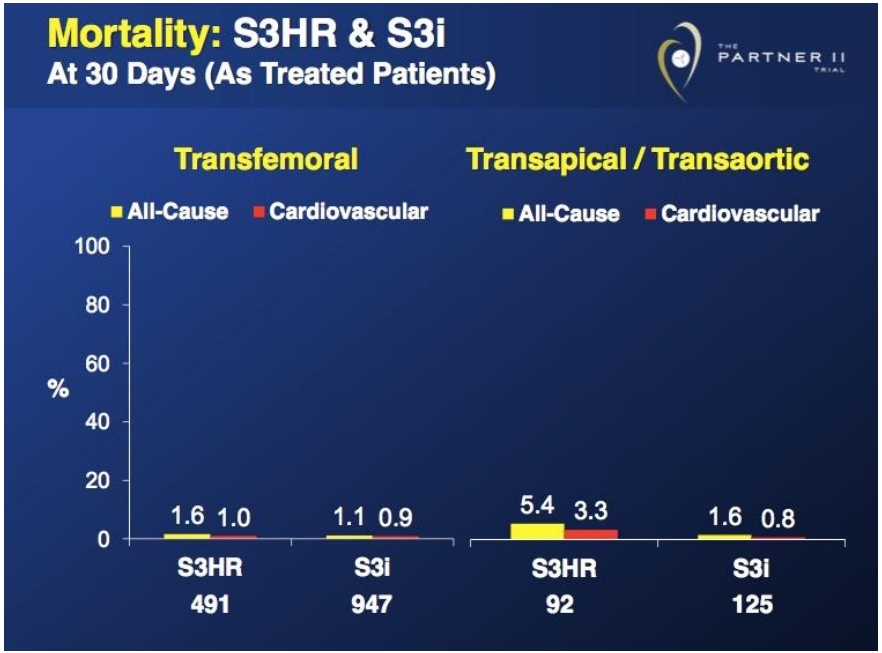


TAVR State of the Art: S3





TAVR State of the Art: S3



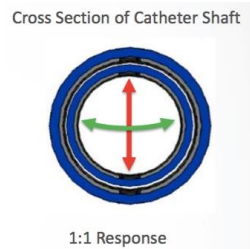
Other Clinical Events
At 30 Days (As Treated Patients)

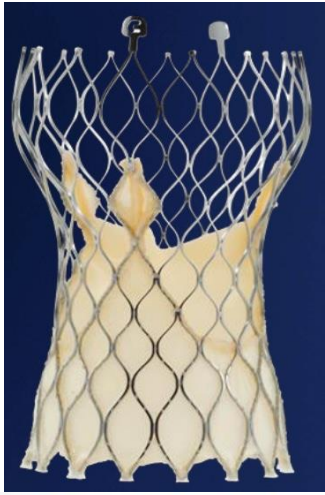
THE PARTNER II TRIAL

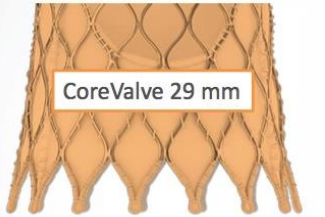
Events (%)	S3HR Overall (n=583)	S3HR TF (n=491)	S3HR TA/TAo (n=92)	S3i Overall (n=1076)	S3i TF (n=951)	S3i TA/TAo (n=125)
Major Vascular Comps.	5.0	5.3	3.3	5.6	5.9	3.2
Bleeding - Life Threatening	6.3	5.5	10.9	5.4	4.4	12.9
Annular Rupture	0.3	0.2	1.1	0.2	0.2	0
Myocardial Infarctions	0.5	0.4	1.1	0.3	0.3	0
Coronary Obstruction	0.2	0	1.1	0.4	0.4	0
Acute Kidney Injury	1.0	0.8	2.2	0.5	0.3	1.6
New Permanent Pacemaker	13.0	13.2	12.0	10.1	10.4	7.2
Aortic Valve Re-intervention	1.0	0.8	2.2	0.7	0.8	0
Endocarditis	0.2	0.2	0	0.1	0.1	0

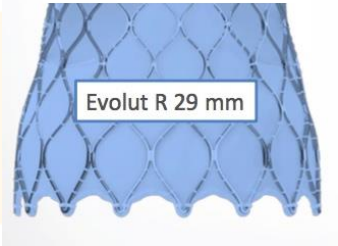
TAVR- State of the Art (Evolute)

- Lower profile (14 fr)
- Recapturable/ Repositionable (at up to 80% deployment)
- Reduced PPM
- Reduced Paravalvular Leak









Evolute CE Mark Study

EVOLUT CE Mark: Purpose

The CoreValve Evolut R CE Clinical Study was designed to assess the safety and clinical performance of the CoreValve Evolut R System (26 mm, 29 mm) in symptomatic extreme- or high-risk patients with aortic stenosis (Heart Team assessment) enrolled at 6 centres in Australia, the United Kingdom, and New Zealand.

Evolut CE Mark: Baseline Demographics

Characteristic, % or mean ± SD	N=60
Age (years)	82.8 ± 6.1
Women	66.7
Body surface area (m^2)	1.7 ± 0.2
STS Predicted Risk of Mortality (%)	7.0 ± 3.7
Logistic EuroSCORE I (%)	20.5 ± 12.5
New York Heart Association class III or IV	68.3
Previous CABG	28.3
Any chronic lung disease	43.3
Diabetes	26.7
Peripheral vascular disease	16.7
Atrial fibrillation / atrial flutter	36.7
Frailty	68.3
Pre-existing permanent pacemaker	11.7

Meredith I EuroPCR 2015

TAVR- State of the Art (Evolute)

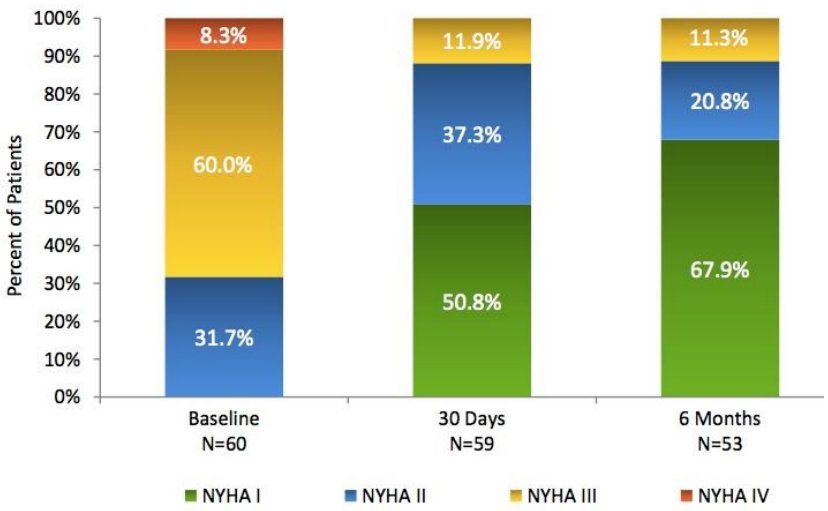
Evolut CE Mark: Safety

Event, K-M rates (no. of patients)	30 Days N=60	6 Months N=60
All-cause mortality	0.0 (0)	5.0 (3)
Cardiovascular	0.0 (0)	3.3 (2)
All stroke	0.0 (0)	1.7 (1)
Disabling	0.0 (0)	1.7 (1)
Non-disabling	0.0 (0)	0.0 (0)
Major vascular complications	8.3 (5)	8.3 (5)
Life-threatening or disabling bleeding	5.0 (3)	8.4 (5)
Embolization or migration	0.0 (0)	0.0 (0)
Endocarditis	0.0 (0)	0.0 (0)
Coronary obstruction	0.0 (0)	0.0 (0)
Valve thrombosis	0.0 (0)	0.0 (0)
Pacemaker*	11.7 (7)	13.4 (8)

*Patients with a prior pacemaker included in the denominator.

Evolut CE Mark: NYHA Class

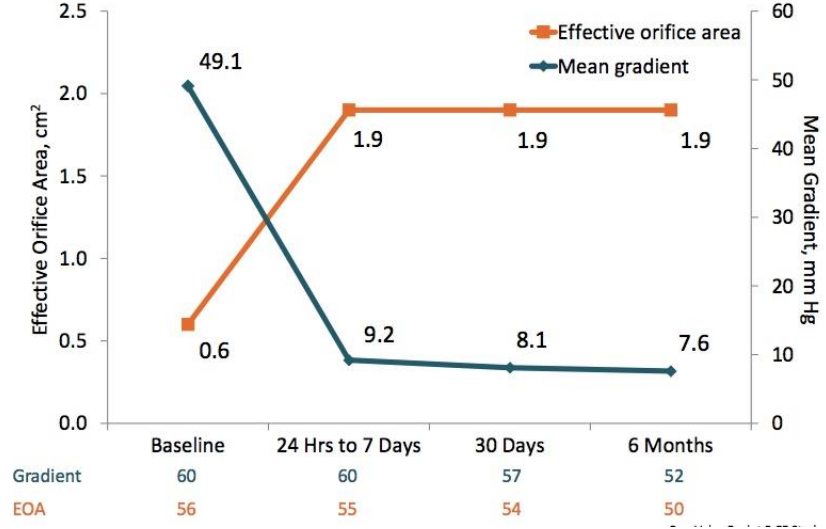
Compared with Baseline, 74.9% Improved at 30 Days and 84.9% at 6 Months



TAVR- State of the Art (Evolute)

euro PCR 2015

Evolut CE Mark: Haemodynamics



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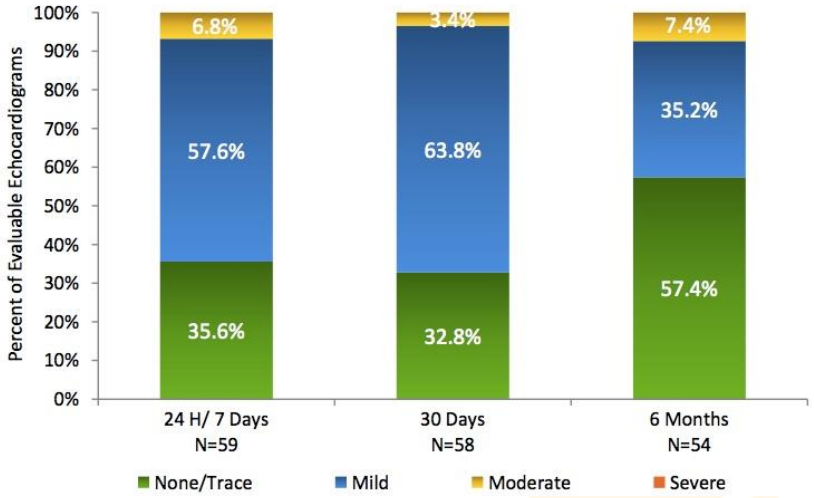
Evolut CE Mark: PVL



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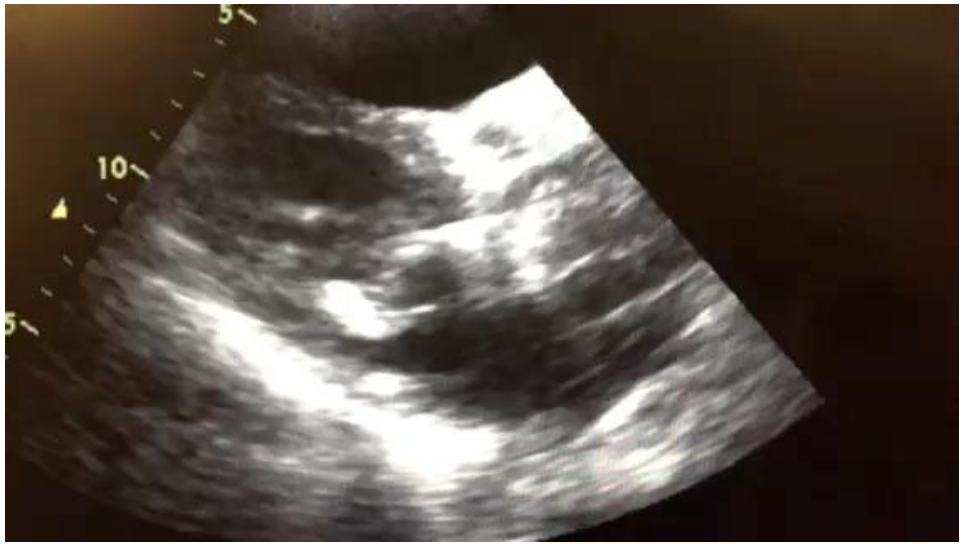
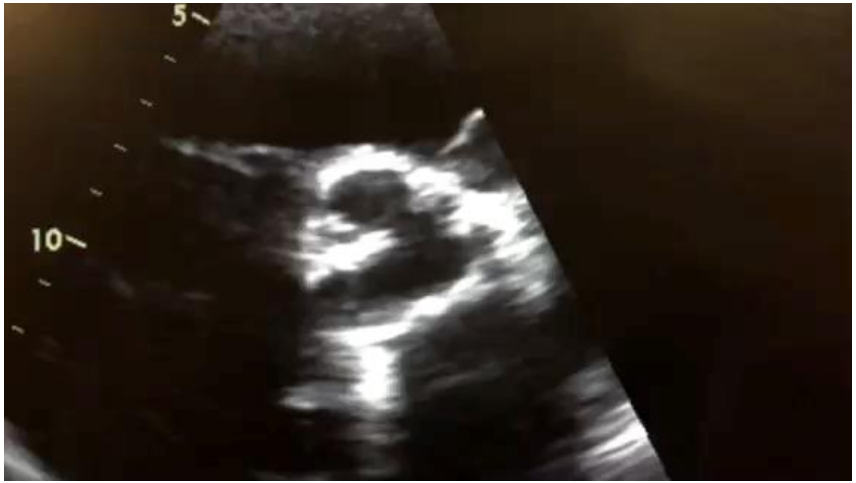
AS Case1

- 74 y/o with Progressive SOB/ Edema.
- Hx CAD/ CABG/ PPM
- Cirrosis/ COPD with active EtOH and Tob



AS Case 1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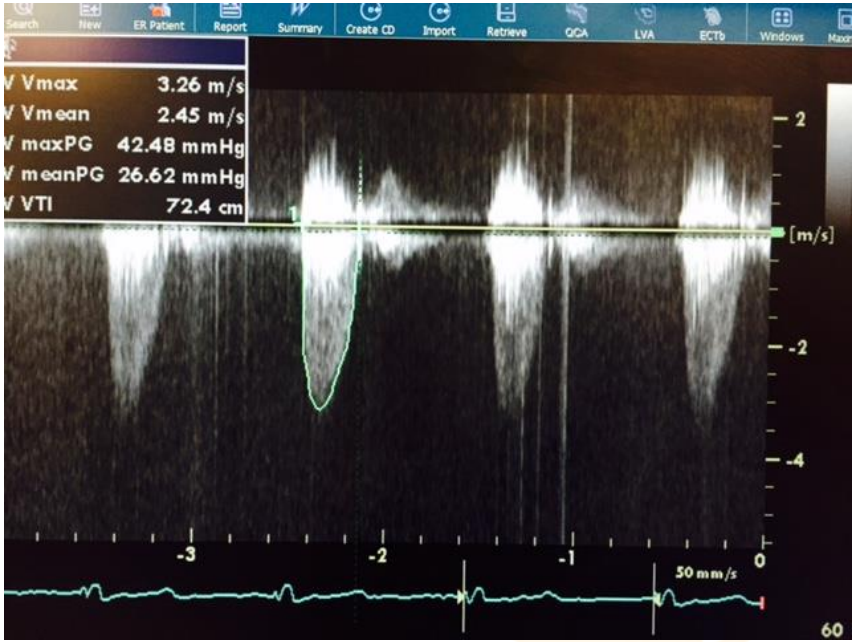
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V Vmax 3.26 m/s
V Vmean 2.45 m/s
V maxPG 42.48 mmHg
V meanPG 26.62 mmHg
V VTI 72.4 cm
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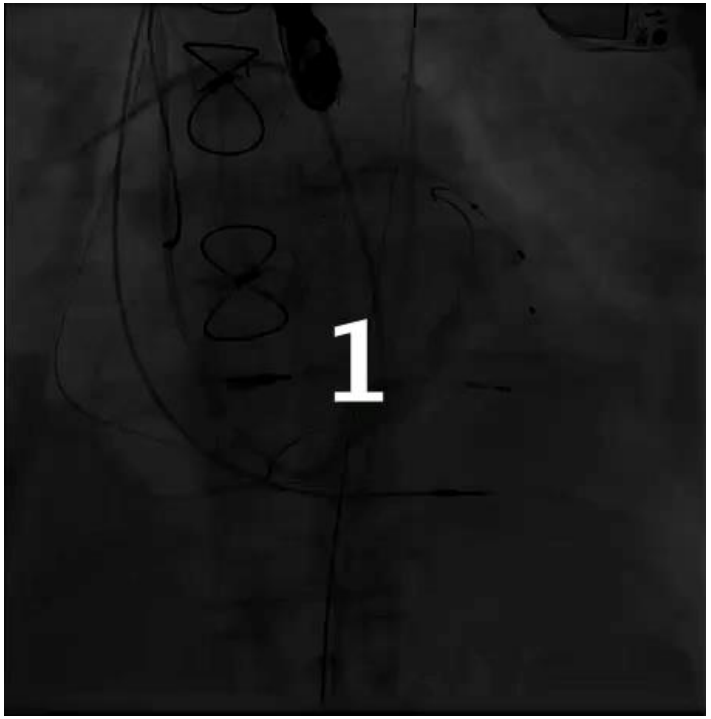
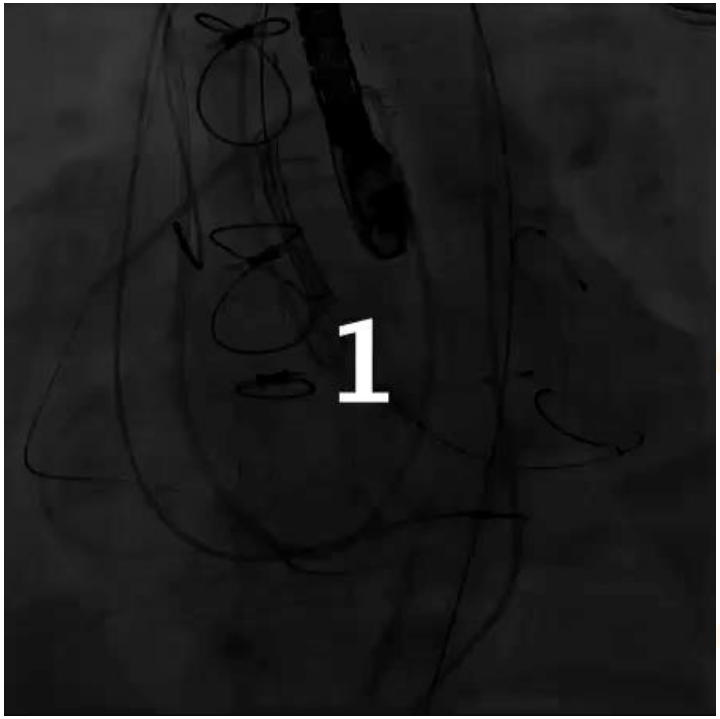
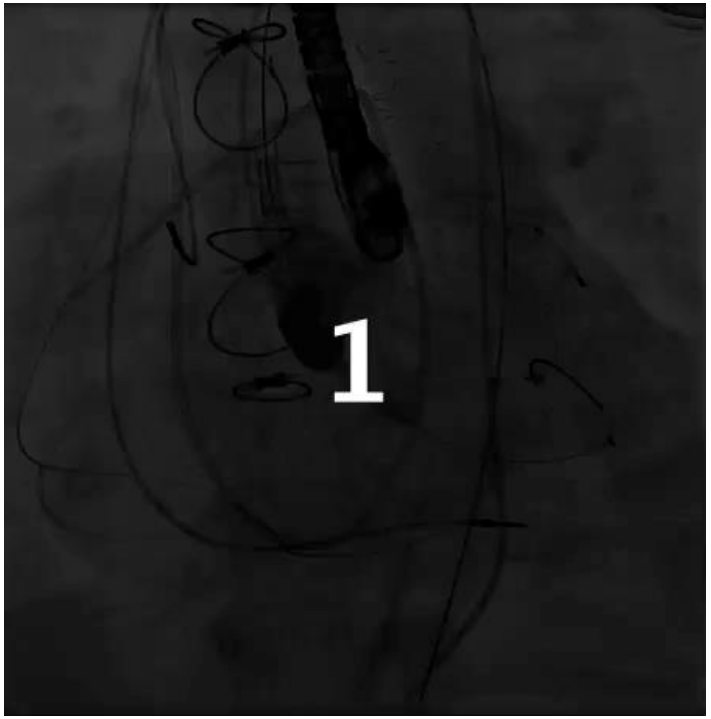
-2
-4
-3
-2
-1
0
50 mm/s
60

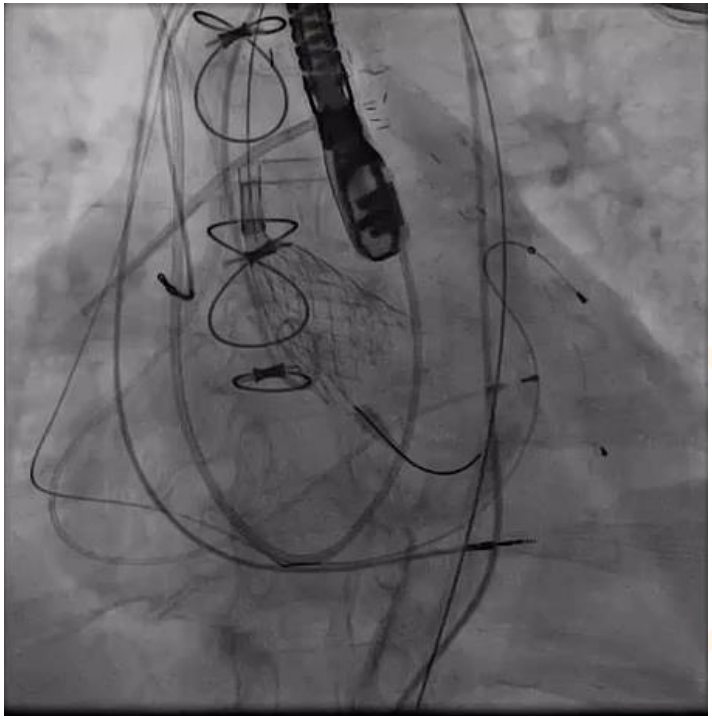
AS Case 1



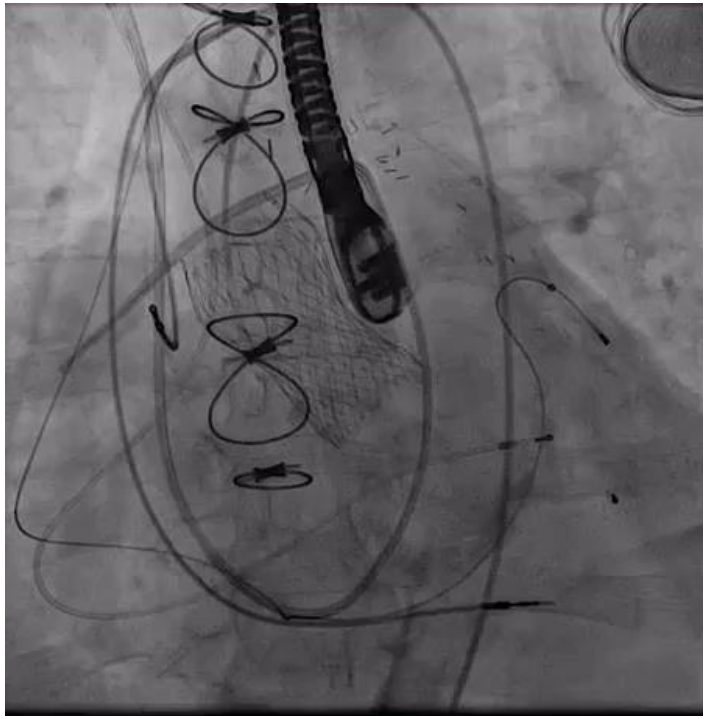


AS Case 1

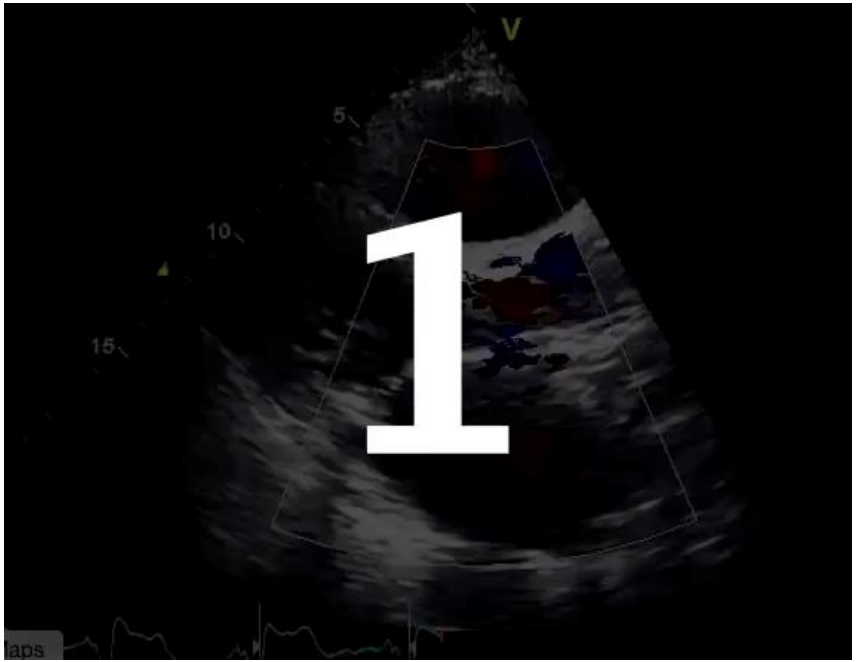


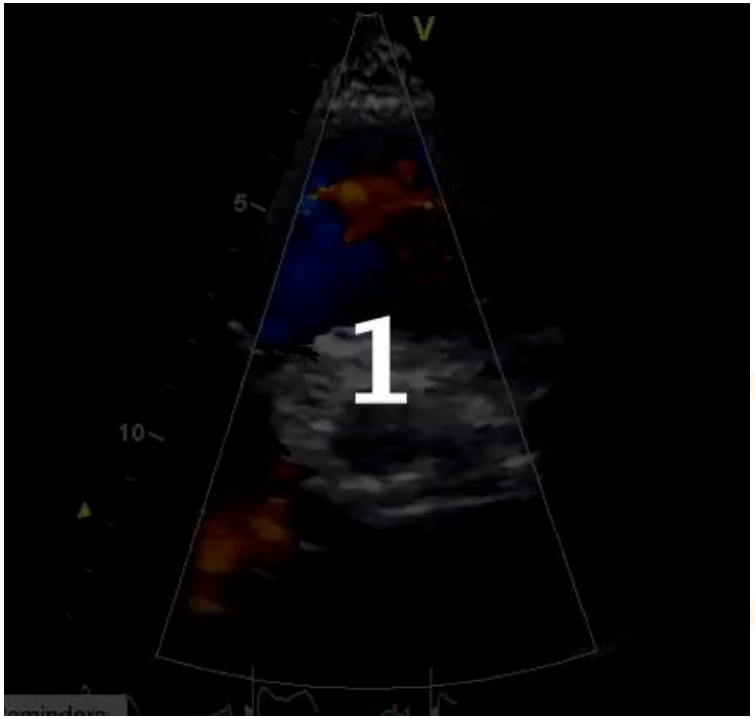


AS Case 1



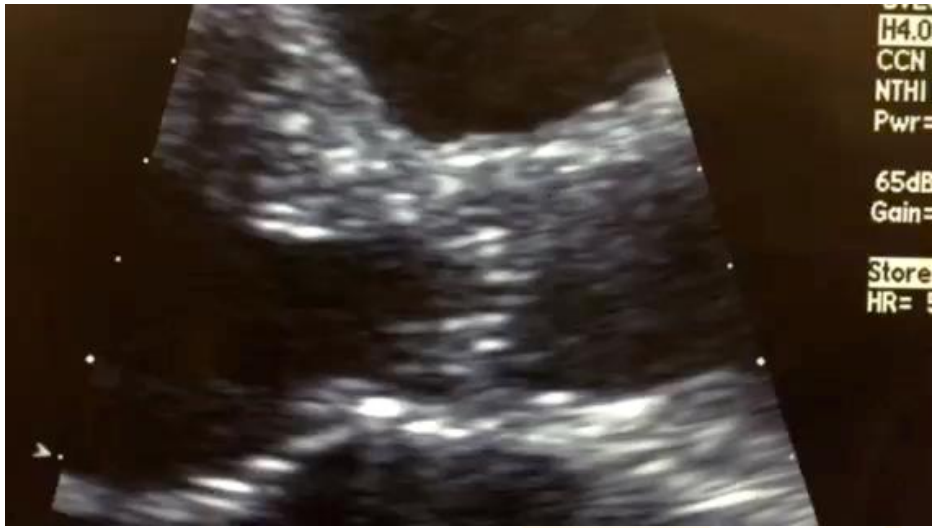
AS Case 1



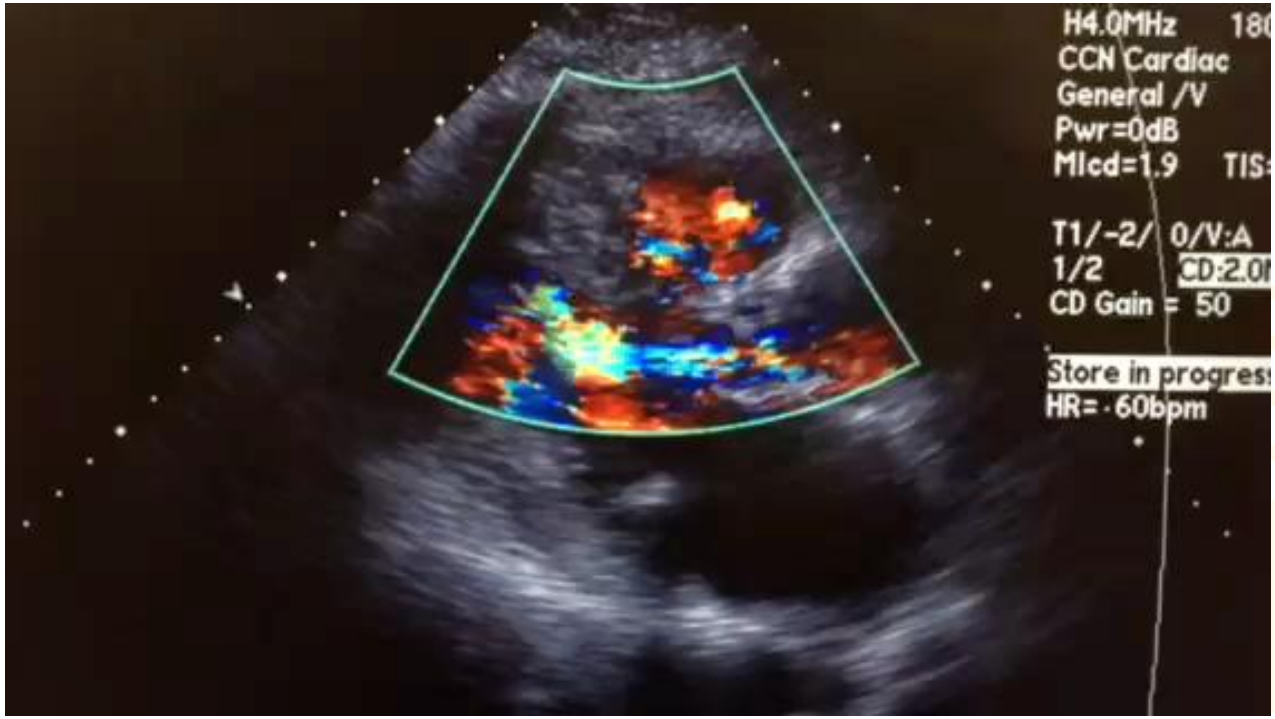


AS Case 2

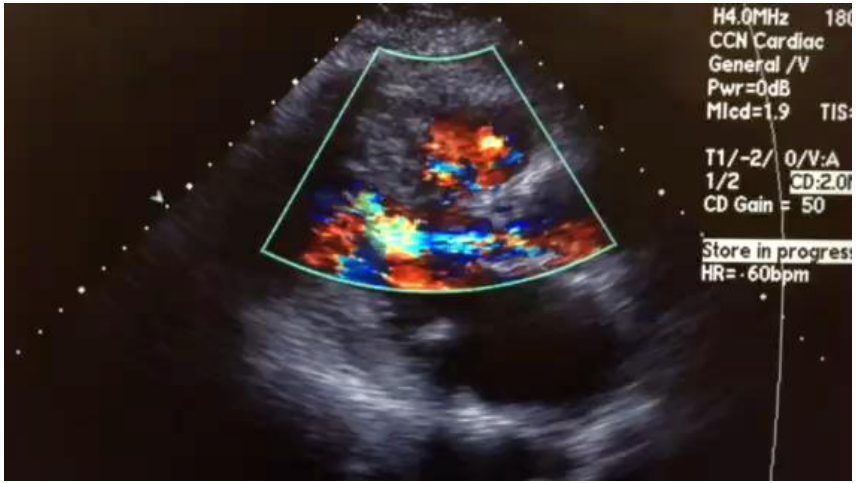
- 76 y/o woman with progressive dyspnea and Edema.
- Hx of Pulmonary HTN.
- Colon Ca dx within the past year.
- On Intermittent Chemotherapy.

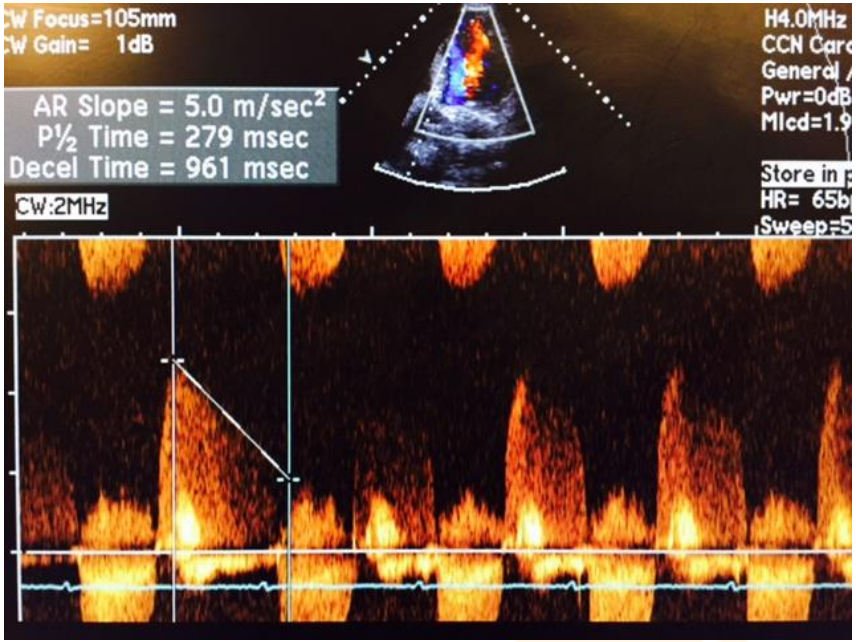


AS Case 2

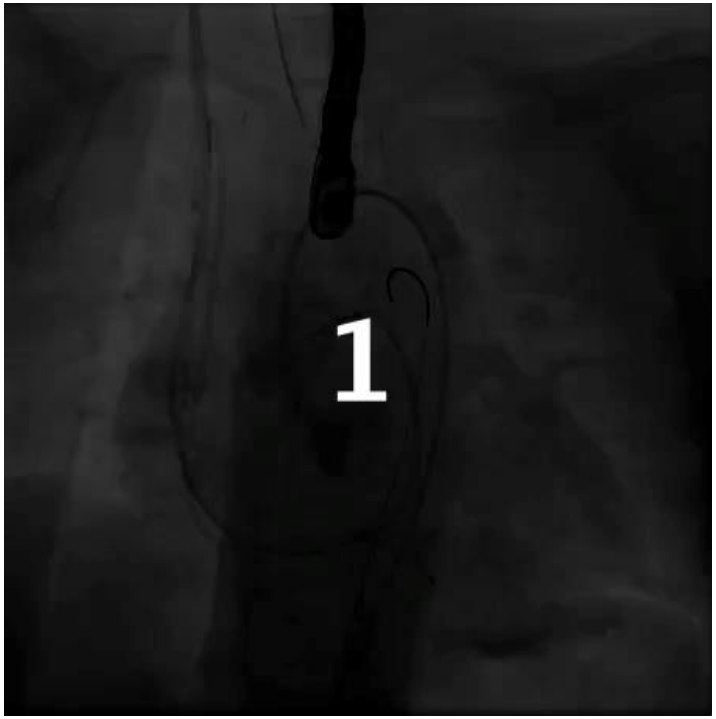

H4.0MHz
CCN Cardiac
General /V
Pwr=0dB
MIcd=1.9
T1/-2/ 0/V:A
1/2
CD Gain = 50
Store in progres
HR= 60bpm

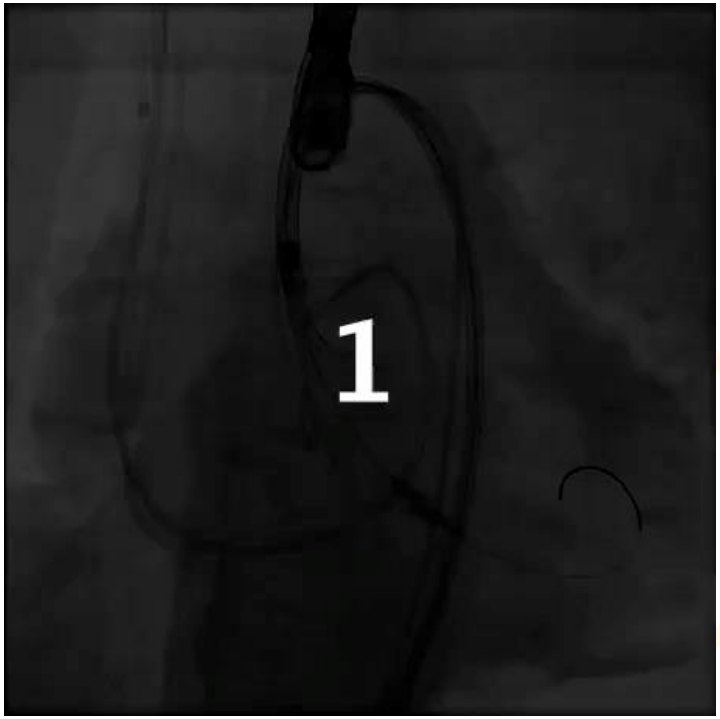
AS Case 2


H4.0MHz
CCN Cardiac
General /V
Pwr=0dB
MIcd=1.9
CD Gain = 50
Store in progres
HR= 60bpm

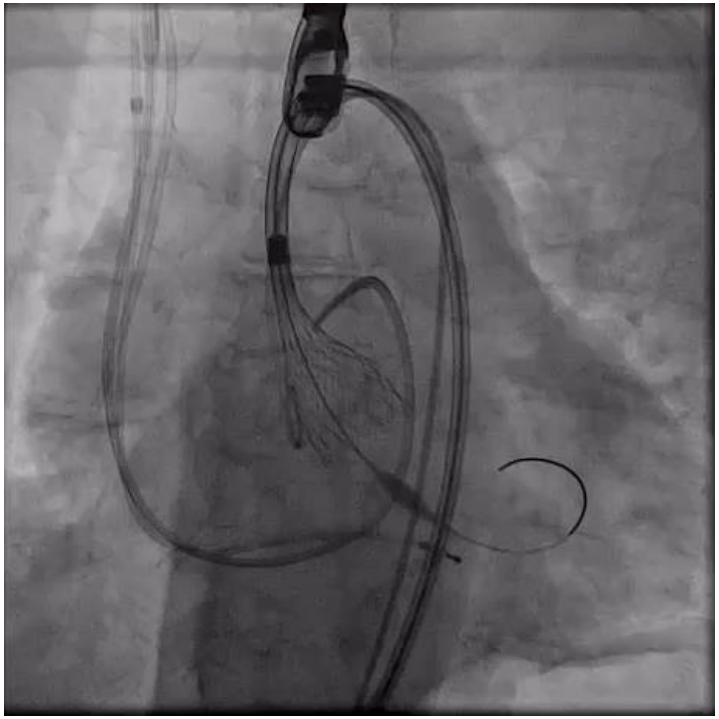

CW Focus=105mm
CW Gain= 1dB
H4.0MHz
AR Slope = 5.0 m/sec²
P½ Time = 279 msec
Decel Time = 961 msec
CW:2MHz
Store in p
HR= 65b
Sweep=5

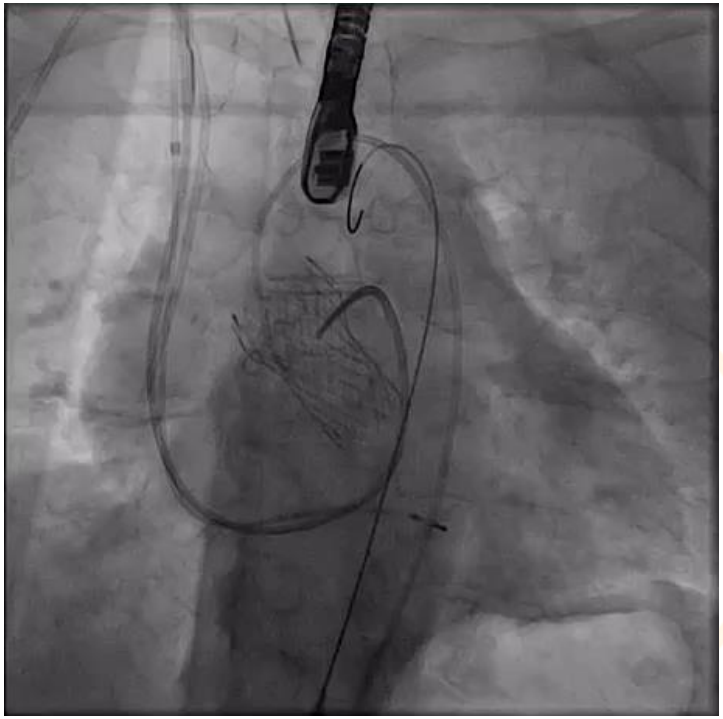
AS Case 2



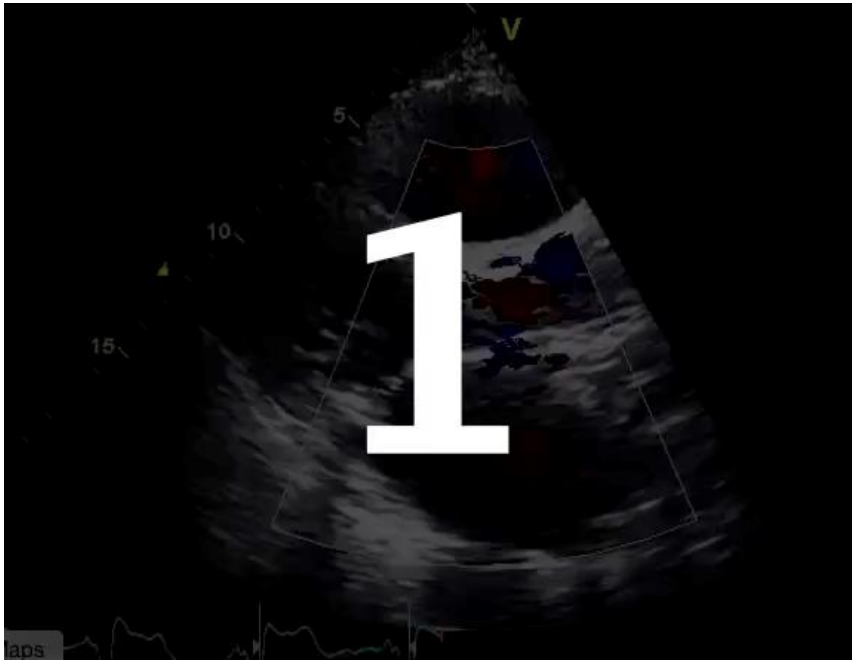


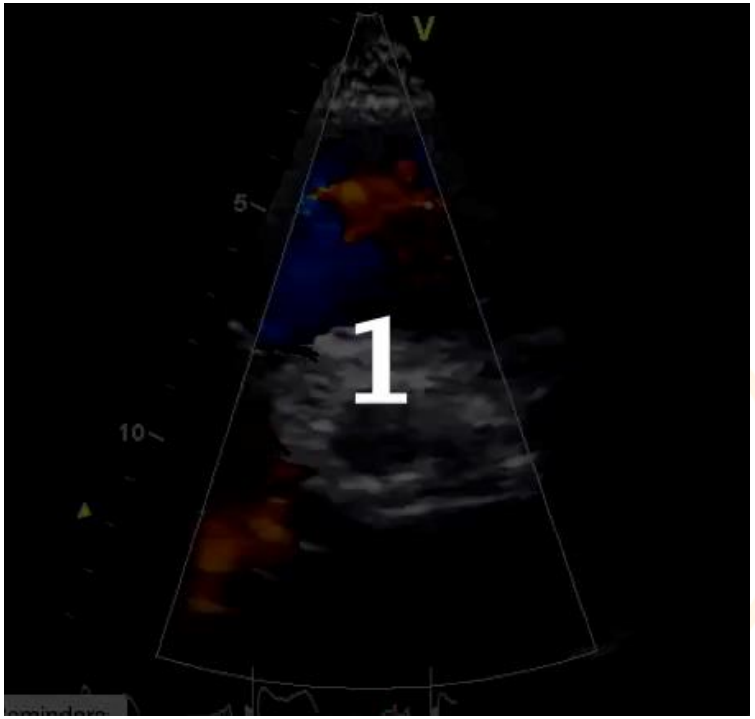
AS Case 2





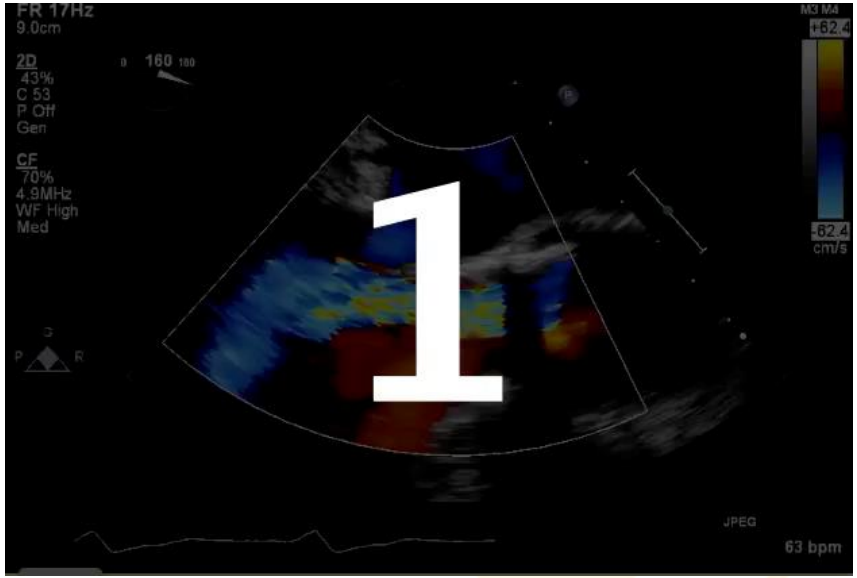
AS Case 2



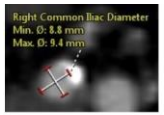


Bioprosthetic Valve Degeneration

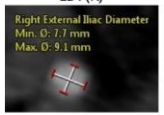
- 84 y/o gentleman with a 12 yr old bioprosthetic valve intially placed for Severe Aortic Stenosis.
- 23 mm Edwards Perimount Valve
- Class 3-4 NYHA class
- EF 35% (dropping)
- Frail (poor candidate for redo sternotomy)
- Large ascending thoracic aorta



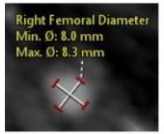
Bioprosthetic Valve Degeneration

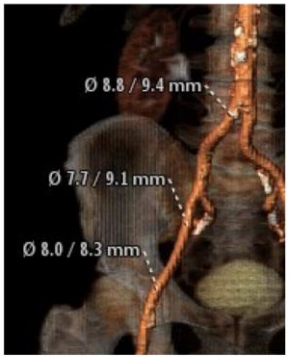


EIA (R)

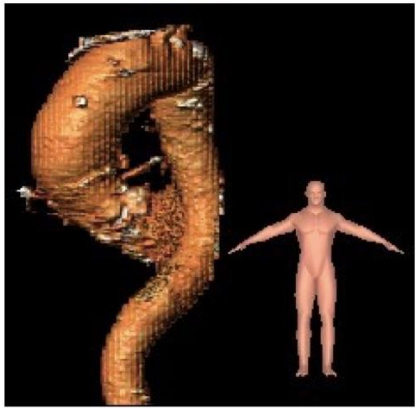


RFA

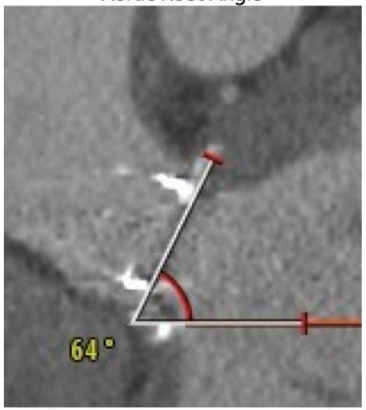




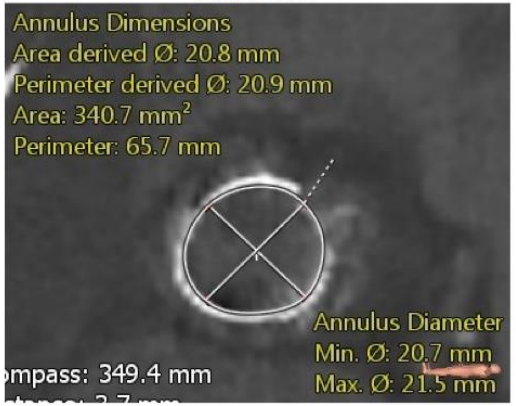
AORTIC ROOT



Aortic Root Angle

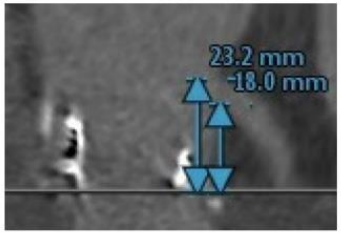


ANNULUS

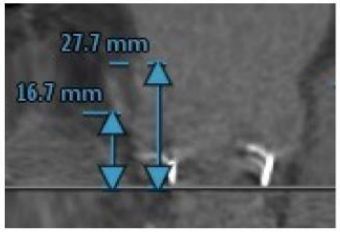


SINUS HEIGHT

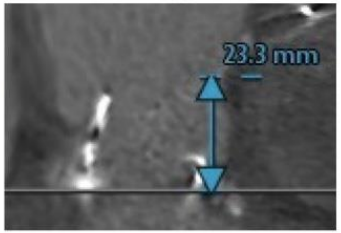
LCC



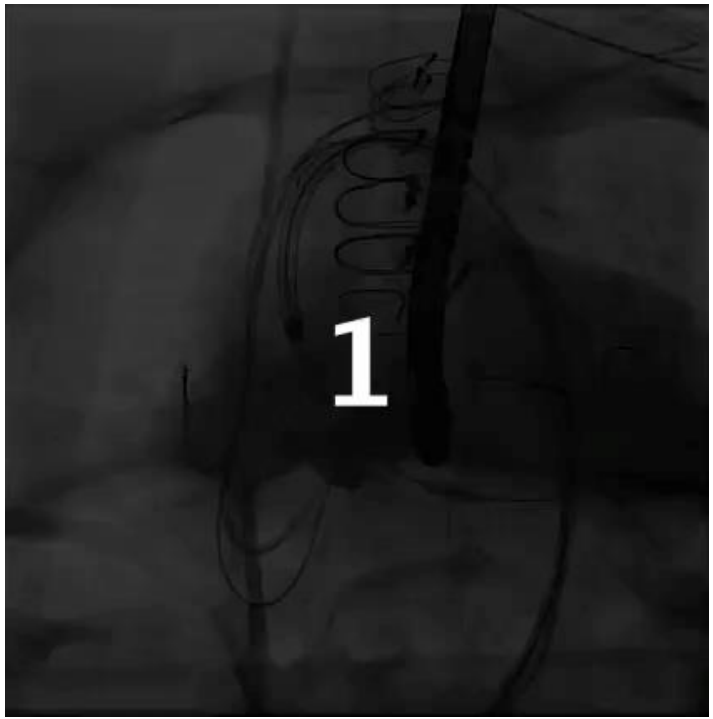
RCC



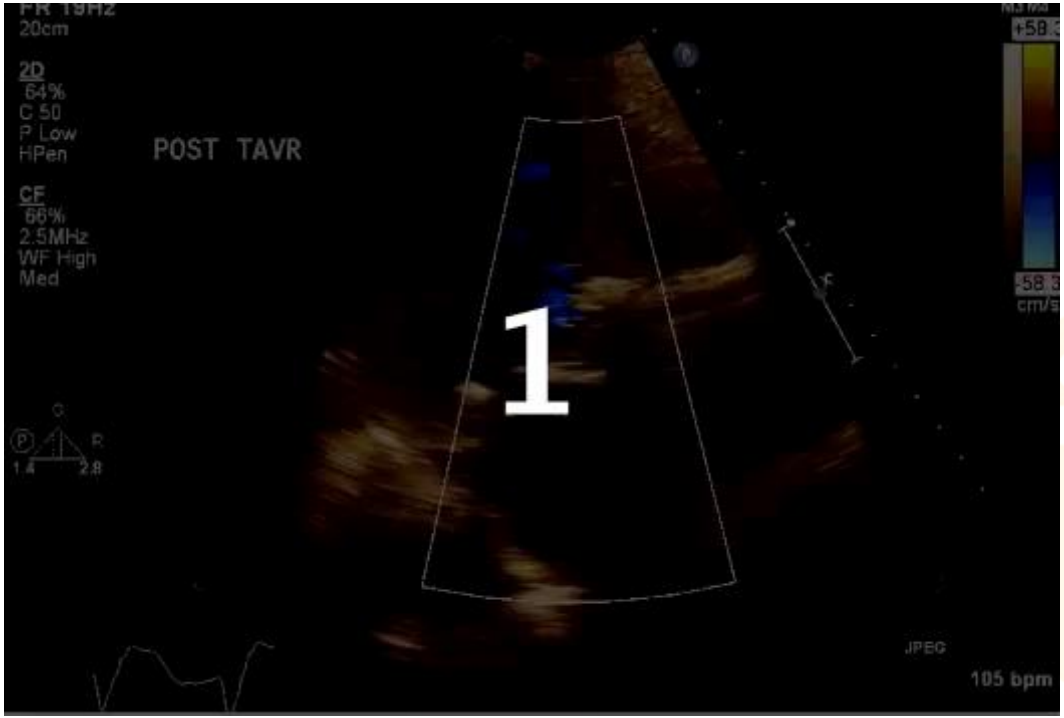
NCC



Bioprosthetic Valve Degeneration



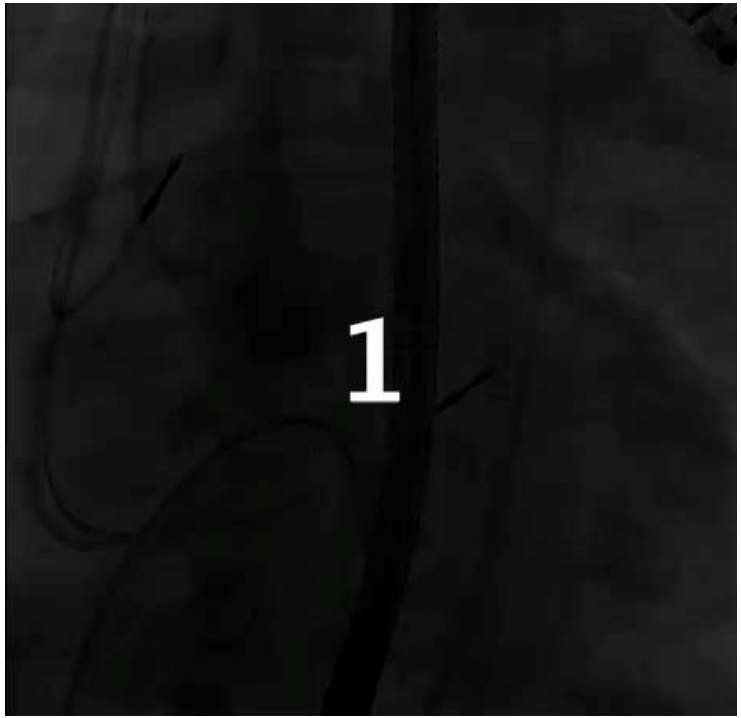
Bioprosthetic Valve Degeneration

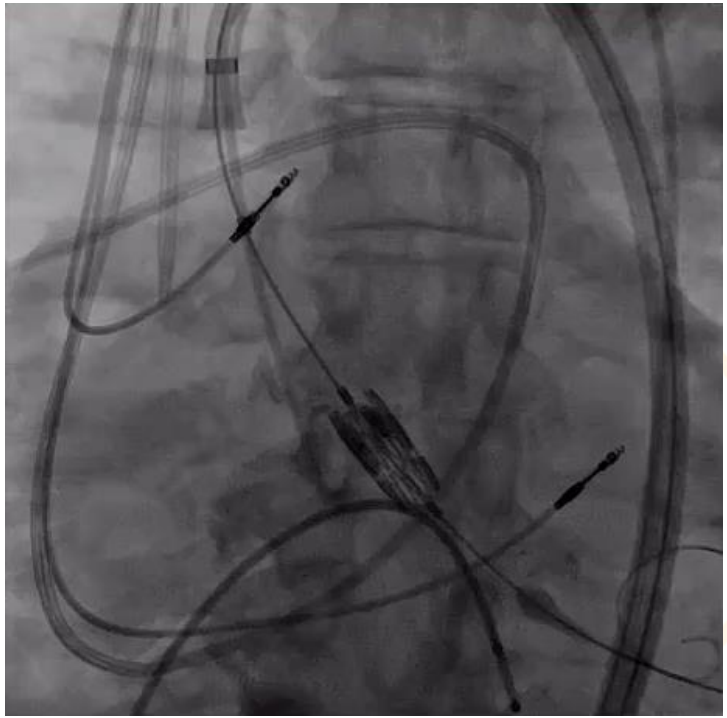


AS Case 3

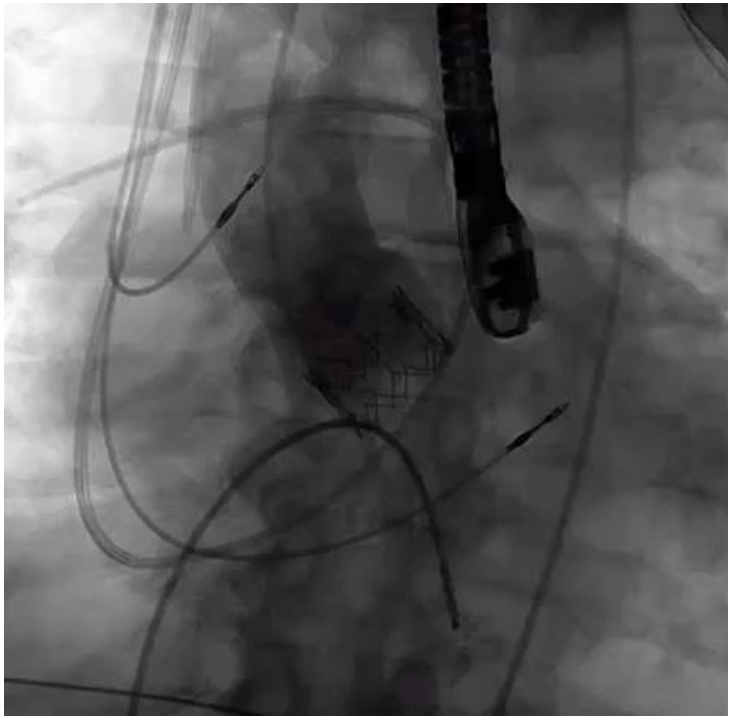
- 79 y/o with severe back pain/ radiculopathy with spinal stenosis.
- Needed urgent back surgery. Found to have Severe AS by echo.
- Mild CAD by Cath
- BAV was done with gradient dropping from 40 mmHg to 20 mmHG and AVA increased from 0.7 to 1.0.
- Pt had uneventful surgery and was brought back for TAVR

AS Case 3

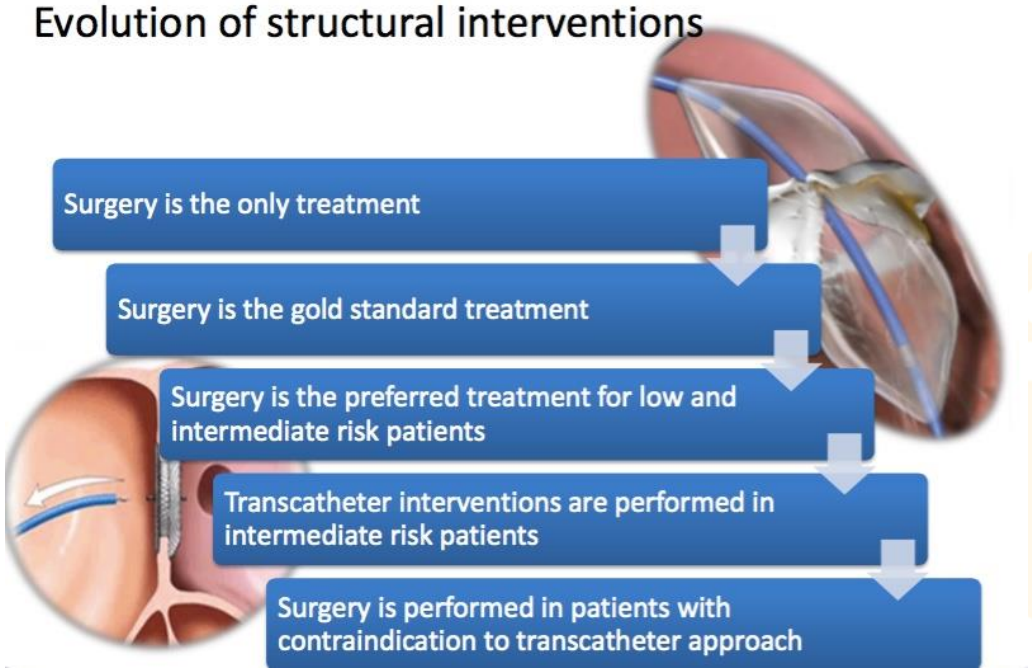




AS Case 3



Thank You



DaVita. | HealthCare Partners.