Major Etiologies for Aortic Stenosis

- Increasing age
- Male gender
- Hypertension
- Smoking
- Elevated LDL cholesterol

Major Risk Factors

Independent clinical factors associated with degenerative aortic valve disease include the following:
- Increasing age
- Male gender
- Hypertension
- Smoking
- Elevated LDL cholesterol
Population at Risk for Aortic Stenosis is Increasing

- Aortic stenosis is estimated to be prevalent in up to 7% of the population over the age of 65.
- Between 1990 and 2020, the US population from 65 - 74 years will increase 74%.
- Currently, 38,000 Alaskans over 70yo, by 2042 est. 120,000.
- In Alaska population over age 75 will triple in next 30 yrs.

Signs and Symptoms

- Heart Failure
- Angina
- Syncope
- Carotid Parvus et Tardus
- Laterally displaced PMI
- Soft A2
- Crescendo-Decrescendo systolic murmur
- Timing of peak murmur predicts severity

Aortic Stenosis Is Life Threatening and Progresses Rapidly

- Survival after onset of symptoms is 50% at 2 years and 20% at 5 years.
- Surgical intervention for severe aortic stenosis should be performed promptly once even minor symptoms occur.
Prognosis

5-Year Survival:

- Breast Cancer: 22%
- Lung Cancer: 17%
- Colorectal Cancer: 30%
- Prostate Cancer: 28%
- Cancer Survival: 20%

5 year survival of breast cancer, lung cancer, prostate cancer, colorectal cancer and severe inoperable aortic stenosis.

Multiple Modalities May Be Used to Diagnose Severe Aortic Stenosis

- Auscultation
- Trans-Thoracic Echo (TTE)
- Chest X-ray
- Electrocardiogram
- Cardiac Cath.
- Auscultation

6 Multiple Modalities May Be Used to Diagnose Severe Aortic Stenosis

Using constant hazard ratio. Data on file, Edwards Lifesciences LLC. Analysis courtesy of Murat Tuczu, MD, Cleveland Clinic.
Echocardiographic Guidelines are the Gold Standard in Assessing Severe Aortic Stenosis

According to the 2014 ACC/AHA guidelines, severe aortic stenosis is defined as:

- Aortic valve area (AVA) less than 1.0 cm²
- Mean gradient greater than 40 mmHg or jet velocity greater than 4.0 m/s

Paradoxical Low Flow and/or Low Gradient Severe Aortic Stenosis

- Dobutamine stress echocardiography can be used to differentiate true from pseudo severe aortic stenosis
  - Better define the severity of the aortic valve
  - Accurately assess contractile pump reserve
- Some patients with severe aortic stenosis based on valve area have a lower than expected gradient and normal or elevated LV function (e.g., EF > 50%)
- Up to 35% of patients with severe aortic stenosis present with low gradients
  - These low gradients often lead to an underestimation of the severity of the disease
  - Many of these patients do not undergo surgical aortic valve replacement

Aortic Valve Replacement Greatly Improves Survival

- Study data demonstrate that early and late outcomes were similarly good in both symptomatic and asymptomatic patients
  - Among asymptomatic patients with AS, omission of surgical treatment was the most important risk factor for late mortality
Options for Aortic Valve Replacement

Tilting Disc Valve

Bio-prosthetic Valve
Studies show at least 40% of patients with severe AS are not treated with an AVR.

What is TAVR—Transcatheter Aortic Valve Replacement?
- An aortic valve replacement as an alternative to traditional thoracotomy.
- Less invasive than traditional thoracotomy currently reserved for patients considered high risk for traditional surgery.

Alain Cribier: First Human Transcatheter Valve Replacement (2002)
Two TAVR Options

- Edwards Sapien 3 Valve
- Stainless Steel Frame
- Better for severe bulky calcification.

- Medtronic CoreValve
- Nitinol Frame - self-expanding
- Less Aortic Regurg, More heart block/PPM

Transfemoral Procedural Animation

PARTNER Study Design

Cohort A
- N = 595
- Transapical (TA)
- Primary Endpoint: All-Cause Mortality at 1 yr (Non-inferiority)
- N = 248
- Transfemoral (TF)
- Co-Primary Endpoint: Composite of All-Cause Mortality and Repeat Hospitalization (Superiority)

Cohort B
- N = 300
- Transapical (TA)
- Primary Endpoint: All-Cause Mortality
- Transfemoral (TF)
- Co-Primary Endpoint: Composite of All-Cause Mortality and Repeat Hospitalization

IN Helix Evolut R: Utilization in 1 yr (Non-inferiority)

Total = 1,395 patients

Inoperable

Standard Therapy

ASSESSMENT:

Symptomatic Severe Aortic Stenosis

High-‐Risk AVR Candidate

PARTNER: 3,105 Total Patients Screened

Total = 1,057 patients

2 Parallel Trials: Individually Powered

Cohort A: High Risk

Cohort B: High Risk

ASSESSMENT:

Transfemoral Access

ASSESSMENT:

Transfemoral Access

1:1 Randomization

Yes

No

Cohort A

Cohort B

TF TAVR

AVR

VS

VVS

N = 179

N = 179

N = 244

N = 104

N = 103
**Partner Trial**

- **All-Cause Mortality (%):**
  - Standard Rx (n = 179): 30.7%
  - TAVR (n = 179): 50.8%

- **Medication Improvement:**
  - Standard Rx: 64.1%
  - TAVR: 87.5%

- **HR [95% CI]:** 0.50 [0.39, 0.65]

- **p (log rank):** < 0.0001

*In an age and gender matched US population without comorbidities, the mortality at 5 years is 40.5%.

**Median Survival**

- **Standard Therapy:** 11.1 Months
- **TAVR:** 29.7 Months

**Cohort B HF Improvement**

**THE PARTNER TRIAL COHORT B**
Mean Gradient & Valve Area

Complications

Reduction in Vascular Complications

Major vascular complications reduced by 25% with next generation device
Cohort A: All-Cause Mortality

The PARTNER 2A and S3I Trials

Study Design

Intermediate Risk Symptomatic Severe Aortic Stenosis

ASSESSMENT by Heart Valve Team

TF TAVR

SAPIEN 3

TA/Tao TAVR

SAPIEN 3

Primary Endpoint: All-Cause Mortality, All Stroke, or Mod/Sev AR at One Year
(Non-inferiority Propensity Score Analysis)

SAPIEN Platforms in PARTNER

Valve Technology

SAPIEN

SAPIEN XT

SAPIEN 3

Surgical AVR

Surgical AVR

1:1 Randomization

Yes

No

TF TAVR

SAPIEN XT VS

VS

TA/Tao TAVR

SAPIEN 3

Sheath Compatibility

Available Valve Sizes

22-24F 22-24F 16-20F 16-20F 14-16F 14-16F
Unadjusted Clinical Events
At 30 Days and 1 Year (AT)

<table>
<thead>
<tr>
<th>Events (%)</th>
<th>30 Days</th>
<th>1 Year</th>
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<tbody>
<tr>
<td>Death</td>
<td></td>
<td></td>
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<tr>
<td>All-cause</td>
<td>1.1</td>
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<tr>
<td>Cardiovascular</td>
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<tr>
<td>Neurological Events</td>
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<td></td>
</tr>
<tr>
<td>All Stroke</td>
<td>1.6</td>
<td>4.4</td>
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<tr>
<td>All-cause Death and Disabling Stroke</td>
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<td></td>
</tr>
<tr>
<td>2.7</td>
<td>6.1</td>
<td>8.4</td>
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</tbody>
</table>

Mortality

Stroke

Number at risk: 1077 1043 1017 991 963 944 859 836 808 795

Number at risk: Sapien 3 TAVR 5/3/2017
Paravalvular Leak

- Significant difference with surgery
- 25-50% have mild or greater PVL
- Newer devices <5%
- Mod AI in TAVR pts carries poor prognosis
- Careful valve sizing decreases risk of significant PVL
Case Presentation

- HS 94 yo male
- Offered evaluation at TAVR center 2013, 2014
- Unwilling to travel outside for evaluation/treatment
- Very willing to undergo eval and treatment here

### TVT Registry

<table>
<thead>
<tr>
<th></th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
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<tr>
<td>Number</td>
<td>4627</td>
<td>9052</td>
<td>16927</td>
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<td>30d Mortality</td>
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<td>7.1</td>
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<td>30d CVA</td>
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<td>Major bleed</td>
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<td>12.0</td>
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<td>&gt;Mild AR</td>
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<td>6.6</td>
<td>7.3</td>
<td>6.2</td>
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<tr>
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<td>98</td>
<td>93</td>
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10.1016/j.acc.2016.11.033
Who Qualifies for TAVR?

- Symptomatic aortic stenosis
  - AVA < 1 cm AND
  - Mean AV gradient >40
  - Peak AV velocity > 4 m/s
- Intermediate-high risk for standard AVR
  - STS > 3
- Estimated life expectancy of >1 yr
TAVR Evaluation

- Echo, carotid duplex, CTA heart, CTA abdominal aorta, ECG
- Coronary angiogram
- Sizing: CTA/echo
- Clinical evaluation by 2 CV surgeons, 1 cardiologist
- Review at multidisciplinary valve conference

Siemens Flash Dual Source CT

- Can scan entire heart in single heart beat
- Markedly improved spatial resolution
- Decreases artifact from arrhythmia
- 75% reduction in radiation
- Operational 3/17
**TAVR in Alaska**
- First cases done April 2015
- Majority of initial patients were extreme risk/non-surgical candidates
- Median length of stay 2d
  - Procedure times < 45 mins.
- Future:
  - Expanding patient population including intermediate risk (9/16), low risk trial underway
  - Move procedure to cath lab from OR

**TAVR Patients**
- 2015: 43
- 2016: 38
- 2017: 25
- Total: 126

<table>
<thead>
<tr>
<th>Type of TAVR Valve</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
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<tr>
<td>Edwards Sapien XT</td>
<td>25</td>
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<td></td>
<td>25</td>
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<tr>
<td>Edwards Sapien 3</td>
<td></td>
<td>92</td>
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<td>92</td>
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<tr>
<td>Medtronic Valves</td>
<td>10</td>
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<tr>
<td>VIV patients</td>
<td></td>
<td></td>
<td></td>
<td>10</td>
</tr>
</tbody>
</table>

Change from Sapien XT to Sapien 3/6/15 (sheath size decreased)
TAVR approved for intermediate risk 9/8/16

**Anesthesia**
- General: 59
- Conscious sedation: 67

**TVT Registry**
- Distribution of hospital performance
- 100% of hospitals met performance benchmarks
- Most hospitals demonstrated improvement in outcomes over time
Length of Stay

- 2016 vs 2015 vs 2014 vs 2012

Procedure Time

- Procedure time is from the time of Lidocaine injection to the time the patient leaves the OR room.

Complications for 2016

- Complications In Hospital
  - 1 Pacemaker
  - 3 minor vascular complication
  - 1 retroperitoneal bleed
  - 1-2 upc transfusion
The Future

Valve-in-valve

- Transcatheter repair of degenerated bioprosthetic surgical valve
- Indicated for bioprosthetic failure by stenosis or regurgitation
- Expanding usage of bioprosthetic valves in younger patients
Following Patient Referral, the TAVR Team will Perform Further Evaluation

1. Confirm the patient is diagnosed with severe symptomatic native aortic stenosis
2. Confirm the patient has been independently evaluated by two cardiac surgeons and meets the indication for TAVR
3. Evaluate the aortic valvular complex using echocardiography
4. Evaluate the peripheral vasculature and aortic valvular complex using MDCT
5. Evaluate the peripheral vasculature and aortic valvular complex using catheterization

Note: Evaluation using CT is typically not done unless the Heart Team confirms that patient is a candidate for TAVR

Aortic Stenosis and TAVR
Aortic Stenosis and TAVR

Key Takeaways

- Aortic Stenosis is prevalent with a high morbidity and mortality when symptomatic and aortic valve replacement is the only treatment associated with improved outcomes.
- Symptomatic (and some asymptomatic) low risk patients will benefit from surgical AVR.
- TAVR is a safe and effective alternative to traditional aortic valve surgery.

Thank You!