An Update of Valvular Heart Disease, 2009

Richard J. Leone, MD, PhD, FACS, FACC
St. Joseph
Cardiothoracic Surgery Associates
Bellingham, Washington
Richard J. Leone, MD, PhD has no commercial interest/conflicts

Images and video supplied by several vendors will be included for demonstration of new technology
Overview

• History of Valve Development
• Applications of Current Valve Technology
• Current Recommendations for Valve Replacement and Repair
• Future of Valvular Surgery
HISTORY OF VALVE DEVELOPMENT
The Early 1900s: The Origins of Prosthetic Heart Valves

- A desire to alleviate valve stenosis and insufficiency was the primary impetus for heart valve technology development
- Stenosis was the primary pathology treated by cardiac surgeons
- Early efforts focused on alleviating symptoms of valve disease rather than valve replacement
The 1920s: Mitral Valve Manipulation

- Once stenosis was realized to be a valvular disease, several physicians performed mitral valve operations.

Dilating a Stenotic Valve with a Finger
The 1920s: Mitral Valve Manipulation

- In 1929, J. H. Powers, M.D. demonstrated that mitral insufficiency was detrimental to hemodynamic flow.
- Research showed that patients treated with finger dilatation fared better than those who received valvotomy.
- Enthusiasm for valvular surgery diminished.
The 1930s and 1940s: Improvement in Surgical Procedures

Advancements contributing to heart valve technology included:

- Hemodynamic data were obtained from patients with stenotic valves.
- Bernard Fantus, M.D. established the first blood bank in 1937.
- Heparin was refined so that it could be used as an anticoagulant.
The 1950s: The First Prosthetic Heart Valves

Mechanical and tissue valves emerged

Mechanical valves:
- Were durable
- Required lifelong anticoagulant treatment
- Sometimes resulted in thrombosis

Tissue valves:
- Had limited durability
- Had relatively little thrombosis
The 1950s: The Ball Valve

- Charles Hufnagel, M.D. implanted the first ball valve in 1952 to relieve a case of aortic insufficiency.
- He implanted the valve into the descending aorta to supplement the native valve.
The 1950s: The Ball Valve

Blood Flow Through a Native Valve

Blood Flow Through a Ball Valve
The 1950s: First Use of Cardiopulmonary Bypass

- John Gibbon, M.D. performed the first successful CPB procedure in 1953.
- Surgeons could see inside the heart clearly and operate for longer periods of time.
- Cardiac surgery was rejuvenated.
The 1950s: Prosthetic Valve Development

Prosthetic valve development had to address three major issues:

- **Hemodynamics**—Determine the efficiency of a prosthetic valve
- **Durability**—Affected by the materials used for the prosthetic valve
- **Thrombosis**—Also affected by the materials used for the prosthetic valve
The 1950s: First Successful Aortic Homograft

- Gordon Murray, M.D. completed the first successful aortic homograft implant
- He implanted the replacement valve into the descending thoracic aorta to supplement the native valve
- The patient enjoyed six years of satisfactory valve function
The 1950s: Original Starr–Edwards Valve

The Starr–Edwards™ valve:

- Consisted of a rigid housing with a PTFE cloth sewing ring
- Had a poppet made of silicone rubber
The 1950s: Current Starr–Edwards Valve

- The current Starr–Edwards valve
- A one-piece cage containing thin struts that meet at the apex.
- A poppet made of silicone rubber with barium sulfate for visibility.
The 1960s: Orthotopic Implants

- An orthotopic valve implant is placed at the same site as the valve it replaces

- The orthotopic implant was a milestone in heart valve technology because the patient depended on the prosthetic valve for survival
The 1960s: Attempts to Refine the Ball Valve

Many physicians attempted to improve upon the ball valve, but they all ran into obstacles.

Experimental valves included:
- Polypropylene disc valve
- Helical spring valve
- Trileaflet synthetic valve
- Bicuspid cloth valve
The 1960s: The Caged-Disc Valve

- The caged-disc valve was developed to improve on caged-ball valves.
- The poppet was replaced with a flat disc to reduce valve profile, but the cage continued to be an obstacle.
The 1960s: The Tilting-Disc Valve

Blood Flow Through a Native Valve

Blood Flow Through a Tilting-Disc Valve
The 1960s: Porcine and Bovine Pericardial Valves

Blood Flow Through a Native Valve

Blood Flow Through a Porcine Valve

Blood Flow Through a Bovine Pericardial Valve
The 1960s: Porcine and Bovine Pericardial Valves

Advantages of porcine and bovine pericardial valves include:

- Obvious similarities to human heart valves
- Easily harvested
- Low rate of thrombosis and hemorrhage related to anticoagulants

The disadvantage of porcine and bovine pericardial heart valves is limited durability
The 1960s: Porcine and Bovine Pericardial Valves

Porcine and bovine pericardial valves:
- Cannot be transplanted in a fresh state
- Have to be preserved and treated with fixing agents to increase the stability of the tissues and decrease antigenicity

Formaldehyde was originally used to preserve tissue, but was later replaced with glutaraldehyde, with better performance.
The Hancock Standard Valve

- The Hancock® Standard valve was the first commercial porcine tissue valve.
- Concerns over high-pressure fixation and development of calcification emerged.
The 1970s: First Bovine Pericardial Valve Replacement

Marian Ionescu, M.D. implanted the first bovine pericardial valve in 1971.

The valves were:
- Constructed from calf pericardium
- Fixed with glutaraldehyde
- Attached to a stent with sutures

Carpentier-Edwards
The 1970s: Bovine Pericardial Valves

• Bovine pericardial valves gained in popularity in the late 1970s and early 1980s because they exhibited excellent hemodynamic properties and low rates of thromboembolism and endocarditis.

• The use of pericardial valves declined when the higher likelihood of structural valve deterioration became apparent.
1970s: Improvements in Tilting-Disc Valves

- In the late 1970s, the Björk-Shiley valve was converted to a convex-concave shape.
- The valve was removed from the market after 400 cases of a broken outflow strut.
1970s: Improvements in Tilting-Disc Valves

Medtronic Hall valve:
- Was introduced in 1977
- Was made from a single block of titanium
- Featured a pyrolytic carbon disc that rotated freely to wear evenly and create two blood flow channels
Medtronic-Hall Mechanical Valve
The 1970s: Bileaflet Valves

The St. Jude Medical bileaflet valve:

- Was introduced in 1977
- Was the first commercially successful bileaflet valve
- Features an occluder mechanism formed by two semicircular leaflets that cause three separate flow areas
St. Jude Regent Valve
The 1980s: Second-Generation Porcine Valves

Characteristics of 2nd-generation porcine valves include:

- *Flexible stents*—Improve blood flow
- *Low-pressure fixation*—Attempt to maintain more natural leaflet structure
- *Anticalcification treatments*—Prevent calcification
The 1980s: Refinements to Prosthetic Heart Valves

- Mechanical and tissue valves developed on parallel tracks
- Most advances were a response to previous shortcomings
Comparison of Cadaveric Homograft and Porcine Valve Implants

The reduction in homograft implantation are due to:
- Little competition from porcine valves before 1965
- Reduced use of homografts once porcine valves became readily available
- CryoLife, Inc., with its inception in 1985, began to provide significant numbers of high-quality homografts and reawakened U.S. surgeons to the successful use of homografts
The 1990s: Third-Generation Porcine Valves

The three major developments in third-generation porcine valves were:

- Physiologic pressure fixation
- Alpha amino-oleic acid, a new anticalcification agent
- Removal of the stent
Evolution of Tissue Technologies: Impact on Valve Performance

**Generation**

**First**
- High pressure fixation
- No anti-calcification treatment

_Hancock® M.O._
_Hancock Std._

**Second**
- Low/zero pressure fixation
- Toluidine Blue, T6

_Hancock® II_
_Intact®_

**Third**
- Physiologic Fixation™
- AOA® treatment

_Mosaic®_
_Freestyle®_

No clinical data are available which evaluate the long-term impact of AOA treatment and Physiologic Fixation in patients. The Intact valve is not FDA approved and not available for sale in the U.S.
The 1990s: Stentless Valves

- Removing the stent can result in improved hemodynamics

Medtronic Freestyle® Stentless Valve
The 1990s: Stentless Valves

Advantages of stentless valves include:
- Reduction in transvalvular pressure gradients with the removal of the stent and sewing ring
- Better distribution of mechanical stress

Disadvantages of stentless valves include:
- More difficult to implant than stented valves
- Additional physician training required
Stentless Aortic Valve
Stentless Aortic Valve
APPLICATION OF CURRENT VALVE TECHNOLOGY
Normal Aortic Valve
Aortic Stenosis
Aortic Stenosis: Surgery vs No Surgery

Choice of Prosthesis

- Patient factors
- Patient age
- Comorbid conditions
- Technical aspects
  - Calcified root
  - Small aortic root
Mechanical vs. Biologic

• Mechanical Valves
  – Rare structural deterioration
  – Patient compliance with Warfarin
  – Anticoagulation risk of Warfarin
    • 1-2% cumulative risk/year

• Biological Valves
  – No long term warfarin required
  – Risk of structural deterioration
  – Risk of reoperation
Median Life Expectancy After Prosthetic Valve Replacement
In Years by Age Group and Pathology

Risk Factors for Thromboembolism

• Atrial fibrillation
• Increased left ventricular cavity size
• Regional wall motion abnormality
• Depressed ejection fraction
• Hypercoagulability
• Increased age
Additional Risk factors for Thromboembolism

- Cancer
- Systemic infection
- Diabetes
- Prior event
- IgA against Chlamydia pneumoniae (CP)
- Eosinophilia
- Hypertension
Risk Factors vs. Thromboembolic Events
Relationship Between INR and Efficacy/Safety

• Low-intensity treatment:
  – Efficacy rapidly diminishes below INR 2.0*
  – No efficacy below INR 1.5

• High-intensity treatment:
  – Safety compromised above INR 4

* Effective below 2.5
Hylek, et al, studied the risk of intracranial hemorrhage in outpatients treated with warfarin. They determined that an intensity of anticoagulation expressed as a prothrombin time ratio (PTR) above 2.0 (roughly corresponding to an INR of 3.7 to 4.3) resulted in an increase in the risk of bleeding.

Adapted from: Hylek EM, Singer DE, Ann Int Med 1994;120:897-902
INR below 2.0 results in a higher risk of stroke

Lowest Effective Intensity for Warfarin Therapy for Stroke Prevention in Atrial Fibrillation

<table>
<thead>
<tr>
<th>INR</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.0</td>
<td>1.0</td>
</tr>
<tr>
<td>1.7</td>
<td>2.0</td>
</tr>
<tr>
<td>1.5</td>
<td>3.3</td>
</tr>
<tr>
<td>1.3</td>
<td>6.0</td>
</tr>
</tbody>
</table>

## Warfarin: Current Indications/Intensity

<table>
<thead>
<tr>
<th>Indication</th>
<th>INR Range</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prophylaxis of venous thrombosis (high-risk surgery)</strong></td>
<td>2.0–3.0</td>
<td>2.5</td>
</tr>
<tr>
<td><strong>Treatment of venous thrombosis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Treatment of PE</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Prevention of systemic embolism</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Tissue heart valves</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>AMI (to prevent systemic embolism)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Valvular heart disease</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Atrial fibrillation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Mechanical prosthetic valves (high risk)</strong></td>
<td>2.5–3.5</td>
<td>3.0</td>
</tr>
<tr>
<td>** Certain patients with thrombosis and the antiphospholipid syndrome**</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>AMI (to prevent recurrent AMI)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Bileaflet mechanical valve in aortic position, NSR</strong></td>
<td>2.0–3.0</td>
<td>2.5</td>
</tr>
</tbody>
</table>
ACC/AHA Guidelines for Postoperative Anticoagulation

• Mechanical Valves
  – Aortic - Warfarin INR 2.0-3.0 (Class I data)
  – Mitral - Warfarin INR 2.5-3.5 (Class I data)

• Biological Valves
  – Aortic - Aspirin (Class I)
  – Mitral – Aspirin (Class I)
    • High-risk pts benefit from Warfarin INR 2.0-3.0 (Class I)
CURRENT RECOMMENDATIONS FOR VALVE REPLACEMENT AND REPAIR
American College of Cardiology/American Heart Association Guidelines for Patients with Valvular Heart Disease

• Class I – Evidence for and/or general agreement that treatment is beneficial, useful and effective

• Class II – Conflicting Evidence
  – IIa Weight of evidence is in favor
  – IIb Efficacy is less well established
ACC/AHA Guidelines  Surgery for Aortic Stenosis Class I

• Symptomatic patients with severe AS (AVA <1.0cm, mean gradient >40 mmHg)
• Patients with severe AS undergoing other heart surgery
• Patients with severe AS and LV dysfunction (EF < 50)
ACC/AHA Guidelines for Surgery for Aortic Stenosis- Class IIb

- Severe AS w/ abnormal response to exercise
- Severe asymptomatic AS w/ likelihood of progressions or if surgery may be delayed at symptom onset (eg. advanced age)
- Asymptomatic pts with very severe AS (AVA < .6, gradient > 60 mmHg)
ACC/AHA Guidelines  Surgery for Aortic Regurgitation - Class I

- Symptomatic pts
- Asymptomatic pts with Severe AR and EF <50
- Severe AR undergoing other heart surgery
- If undergoing Ascending Aorta replacement
- Pts with severe AR and LV dilatation
ACC/AHA Guidelines for Surgery for Mitral Regurgitation

• Mitral Repair is indicated for most patients with Severe MR and Any Symptoms
• Controversy exists with Asymptomatic patients with Severe MR
ACC/AHA Guidelines for Surgery for Mitral Regurgitation – Class I

- Symptomatic pts with Severe MR
- Chronic Severe MR and NYHA Functional Class II, III or IV symptoms
- Asymptomatic pts with Severe MR and EF 30-60%
- Mitral Repair is now recommended over Replacement in majority of pts
ACC/AHA Guidelines for Surgery for Mitral Regurgitation – Class IIa

- MV Repair recommended in Experienced Centers for Asymptomatic pts with Chronic Severe MR and Normal (<60%) EF
- MV Repair for Chronic Severe MR and new onset AF or Pulmonary Hypertension
Mitral Valve Repair

- Mitral Valve was traditionally replaced
- Improved Survival with Repair
- No need for long-term Anticoagulation
Mitral Valve Repair
FUTURE OF VALVULAR SURGERY
Thoracic Aortic Aneurysms
Thoracic Aortic Stent Graft
Transcatheter Valves
Transcatheter Valves

- Tremendous interest in transcatheter valve therapy
- No current FDA Approval for transcatheter valves in US
- Several platforms
- Reserved for highest-risk (nonsurgical) patients
Medtronic CoreValve
**Medtronic CoreValve Transcatheter Valve**

**Catheter insertion**
A valve delivery catheter is inserted in the groin and threaded up to the diseased heart valve.

**Guidance**
Fluoroscopy is used to position the tip of the catheter in the annulus of the aorta.

**Valve deployment**
A new artificial valve mounted in a self-expanding stent is deployed in the aortic annulus.

**Catheter**

**Deploying stent**

The new valve pushes the diseased valve out of the way and anchors itself in place.

**Anchored stent**

**New valve**

**Beating heart**
The patient's heart continues beating.
Edwards Sapien Transcatheter Valve
Transfemoral Insertion

• For patients without obstructive peripheral vascular disease
• Need to negotiate the aortic arch
• Risks and benefits of valve surgery without cardiopulmonary bypass
Transfemoral
Transapical Insertion

- Requires thoracotomy
- Very limited access to the heart but less invasive
- Offers more accurate deployment of valve
Transapical Valve
Transcatheter Valvular Surgery

- Small series show promise
- Technical obstructions remain
  - Proper sizing, valve durability
- FDA approval is currently pending in USA
Transcatheter Mitral Surgery
Transcatheter Mitral Clip
Transcatheter Valvular Therapies

• May further less-invasive valvular repair in the highest-risk patients