WHAT’S NEW IN...

Interventional Cardiology

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DISCLOSURE

• No financial conflicts to disclose
  • I have not received money from any of the companies/products mentioned today
  • I do not have any direct investments in any of the companies/products mentioned today

• I will be discussing two relatively recent technological advances today
  • No discussion of unapproved products/uses
OBJECTIVES

• To provide a general overview of what interventional cardiologists do

• To highlight two interesting advances in the field of interventional cardiology
  • Bioabsorbable stents
  • TAVR (transcatheter aortic valve replacement)
CASE #1

An 82 year old man comes to your clinic with a complaint of exertional chest pressure over the last month.

PMH: Hypertension, dyslipidemia, and atrial fibrillation; no prior MI

Soc Hx: Former smoker – quit 15 years ago (2 ppd x 40 yrs)
   Lives with his wife in Baltimore
Meds: Coumadin, HCTZ, atorvastatin, diltiazem
CASE #1

Exam: Normotensive, HR in the 70's, irregular, breathing comfortably

Unremarkable for physical signs of heart failure, valvular disease, pulmonary disease

EKG: Normal
CASE #1

You are his cardiologist. You recommend the following:

A. Adjustment of medication alone
B. A stress test (as soon as possible)
C. A cardiac catheterization
D. A trial of cardiac rehab
He opts for cardiac catheterization, which shows the following:
CASE #1

As his newly minted cardiologist, you recommend the following:

A. Adjustment of medical therapy alone
B. Implantation of a bare metal stent
C. Implantation of a drug eluting stent
D. Implantation of a bioabsorbable stent
E. Coronary artery bypass surgery
F. Run away from all doctors
INTERVENTIONAL CARDIOLOGY: IT’S MORE THAN “JUST STENTS”

• Coronary artery disease (diagnosis and treatment)
• Peripheral vascular disease (diagnosis and treatment)
• Valvular heart disease (diagnosis and treatment)
• Pulmonary hypertension (diagnosis and evaluation of treatment)
• Cardiomyopathy (diagnosis and treatment)
• Congenital heart disease (diagnosis and treatment)
  • Adult and pediatric
• Cryptogenic stroke
• Pericardial disease
• Other
INTERVENTIONAL CARDIOLOGY: IT’S MORE THAN “JUST STENTS”

- Coronary artery disease (diagnosis and treatment)
  - Stents
- Peripheral vascular disease (diagnosis and treatment)
  - Stents
- Valvular heart disease (diagnosis and treatment)
  - TAVR
  - Valvuloplasty
- Pulmonary hypertension (diagnosis and evaluation of treatment)
  - Right heart catheterization
- Cardiomyopathy (diagnosis and treatment)
  - Right heart catheterization
- Ventricular support devices (IABP, Impella, perc VAD’s)
  - EtOH ablation for HOCM
- Congenital heart disease (diagnosis and treatment)
  - ASD, VSD, PDA closures
  - Fistula embolization
- Pericardial disease
  - Pericardiocentesis
- Cryptogenic stroke
  - PFO closure
- Other
  - LAA closure
BUT WE DO A LOT OF STENTS...
A BRIEF HISTORY/EVOLUTION OF CORONARY INTERVENTION

Table 1 Historical milestones in coronary artery stenting

<table>
<thead>
<tr>
<th>Time</th>
<th>Person(s)</th>
<th>Landmark events</th>
</tr>
</thead>
<tbody>
<tr>
<td>1964</td>
<td>Dotter and Judkins</td>
<td>Conceptual description of coronary angioplasty using an implantable prosthetic device</td>
</tr>
<tr>
<td>May 1977</td>
<td>Gruntzig and Myler</td>
<td>First coronary angioplasty during coronary artery bypass graft surgery</td>
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<tr>
<td>September 1977</td>
<td>Andreas Gruntzig</td>
<td>First coronary angioplasty in an awake patient; a revolution in interventional cardiology</td>
</tr>
<tr>
<td>1979</td>
<td>Geoffrey Hartzler</td>
<td>First balloon angioplasty to treat AMI</td>
</tr>
<tr>
<td>1986</td>
<td>Sigwart and Puel</td>
<td>The first implantation of a stent in human coronary arteries; second revolution in interventional cardiology</td>
</tr>
<tr>
<td>1991</td>
<td>Cannon and Roubin</td>
<td>First coronary stenting to treat AMI</td>
</tr>
<tr>
<td>1994</td>
<td>Serruys et al. and Fishman et al.</td>
<td>Publication of first two landmark (Benestent and STRESS) trials</td>
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<tr>
<td>1994</td>
<td>FDA</td>
<td>FDA-approved use of stents to treat acute and threatened vessel closure after failed balloon angioplasty</td>
</tr>
<tr>
<td>1999</td>
<td>Eduardo Sousa</td>
<td>The first drug (sirolimus) eluting stent implanted in human coronary artery; third revolution in interventional cardiology</td>
</tr>
<tr>
<td>2002–04</td>
<td>EME and FDA</td>
<td>Approvals of Cypher and Taxus stents in Europe and USA</td>
</tr>
<tr>
<td>2011</td>
<td>EME</td>
<td>Approval of Absorb BVS (biodegradable vascular scaffold) in Europe; fourth revolution in interventional cardiology</td>
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FDA, Food and Drug Administration USA; EME, European Medicines Agency.

2016: FDA approves Absorb BVS in U.S.

A BRIEF HISTORY ... SIMPLIFIED

1977 – early 1990s: Plain Old Balloon Angioplasty (POBA)
   - The Good: Opened blockages
   - The Bad: Unacceptable rate of acute (10%) and chronic (50%) repeat blockage

1990s – mid 2000’s: Bare metal stent
   - The Good: Eliminated acute repeat blockage and reduced chronic blockage
   - The Bad: Small risk of stent thrombosis (ST) (1%)
   - Risk of in-stent restenosis (ISR) (20-30%)
Mid 2000’s = present: **Drug eluting stents**

Different than bare metal stents because:
- Have a polymer coating
- Elute a drug that inhibits restenosis

**The Good:** Reduced ISR to 10%

**The Bad:** Risk of ST still present
- Still a residual risk of ISR
THE CASE FOR A BIOABSORBABLE STENT

• **Metal stents:**
  • Are foreign bodies and may lead to ST, which is life-threatening
  • May interfere with normal vascular function (which may lead to ISR?)
  • Cannot be removed once inserted
  • May cover side branches and impede blood flow to them
  • May preclude future coronary artery bypass surgery (CABG)
THE CASE FOR A BIOABSORBABLE (BVS) STENT

• In theory, a bioabsorbable stent would:
  • Dissolve and lower the risk of ST and ISR
  • Dissolve and reduce the need for prolonged dual anti-platelet therapy, which is needed to prevent ST
  • Dissolve and “uncover” side branches
  • Dissolve and restore normal vascular function
  • Dissolve and allow for future CABG

• BVS = Bioabsorbable Vascular Scaffold
BIOABSORBABLE STENTS: HOW DO THEY WORK?

- Made of bioabsorbable material
  - Metallic alloy (not currently in clinical use)
  - Polymer (poly-L-lactic acid and poly-DL-lactic acid)

- Coated with same drug as drug-eluting metallic stents

- Stent is implanted similarly to metallic stents

- Stent dissolves over time
BVS IN PICTURES

www.absorb.com
Metallic DES vs. Absorb BVS

Representative Human images at 5 Years

Metallic DES\textsuperscript{1}  
Absorb-Treated Artery\textsuperscript{2}

\textsuperscript{1}Atherosclerosis 2014;237:23e29
\textsuperscript{2} Images courtesy of S Windecker, ABSORB Cohort B 5 Yrs
ARE BVS “BETTER THAN” OTHER STENTS?

- Is there less stent thrombosis (ST)?
- Is there less in-stent restenosis (ISR)?
- Is there less need for future stent procedures (i.e. “repeat revascularization”)?
- Do they reduce a person’s chance of having a heart attack?
- Do they save lives?
Everolimus-Eluting Bioresorbable Scaffolds for Coronary Artery Disease

Stephen G. Ellis, M.D., Dean J. Kereiakes, M.D., D. Christopher Metzger, M.D., Ronald P. Caputo, M.D., David G. Rizik, M.D., Paul S. Teirstein, M.D., Marc R. Litt, M.D., Annapoorna Kini, M.D., Arneer Kabour, M.D., Steven O. Marx, M.D., Jeffrey J. Popma, M.D., Robert McGreevy, Ph.D., Zhen Zhang, Ph.D., Charles Simonton, M.D., and Gregg W. Stone, M.D., for the ABSORB III Investigators*
ABSORB III: BVS VS. DES

• 2008 patients with stable/unstable angina randomized to:
  • Absorb (bioabsorbable stent) OR
  • Xience (drug-eluting stent)
  • Both release the same drug (everolimus)

• Excluded:
  • Patients with acute MI
  • Patients with complex lesions
"Target Lesion Failure" = death, MI, repeat stenting

Ellis et al, NEJM 2015.
ARE BVS “BETTER THAN” OTHER STENTS?

• Is there less stent thrombosis (ST)? Not in short term – trend toward more ST with BVS

• Is there less in-stent restenosis (ISR)? Not in short term

• Is there less need for future stent procedures (i.e. “repeat revascularization”)? Not in short term

• Do they reduce a person’s chance of having a heart attack? Not in short term

• Do they save lives? No
SO WHY THE FUSS ABOUT BVS?

• ABSORB III basically showed that BVS are “noninferior” to DES in the short term

• Longer term studies are underway to determine if there are long-term benefits to BVS
  • ABSORB IV

• Scientific rationale continues to be: if we can eliminate the foreign body, we may be able to restore normal vessel function and reduce risk of ST/ISR
BACK TO OUR CASE

You determine that your patient needs a stent in the LAD, which will help relieve his exertional angina symptoms. You recommend:

A. Bare metal stent
B. Drug-eluting stent
C. Bioabsorbable stent
QUESTIONS ABOUT BVS
A 91 year old woman comes to your office with complaints of shortness of breath with exertion over the past year.

History of breast cancer with XRT 20 years ago

Walked unlimited distances prior to 1 year ago

Now breathless with cleaning, grocery shopping, climbing stairs
• Exam: 3/6 crescendo decrescendo, late peaking murmur at the RUSB; A2 diminished
  • Delayed carotid pulse
  • S4

• EKG: Sinus rhythm, LVH
You are her cardiologist. You recommend:

A. No further testing because she’s 91 years old
B. No further testing because there’s nothing going on with her heart
C. Immediate cardiac catheterization
D. An echocardiogram
• You recommend, and she agrees to have, an echocardiogram.

• The echocardiogram shows this:
The echocardiogram shows severe aortic stenosis. You recommend:

A. No further therapy because she is 91 years old
B. Surgical AVR
C. Transcatheter AVR (or TAVR)
D. Balloon aortic valvuloplasty
Severe Aortic Stenosis

Traditional therapy:
surgical aortic valve replacement

http://newheartvalve.com/hcp/about-aortic-stenosis
www.phsoregon.org
Aortic Stenosis

Most common valve pathology in the US
Affects 4% of population > age 75 years

Americans are living longer
> 65 years projected to grow from 13% to 20% by 2030
> 85 years projected to triple over next 40 years

Historically elderly AS patients – 1/3rd not offered surgery

FDA-Approved TAVR Devices

Edwards SAPIEN 3

Medtronic Evolut (CoreValve)

Patient Selection: SAVR vs. TAVR?

AS Severity
Symptoms

Surgical Risk Assessment
STS risk calculator
Incremental risk factors
Clinical judgment

riskcalc.sts.org
91 yo woman known severe AS
91 yo woman known severe AS...

<table>
<thead>
<tr>
<th>Risk Score</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk of Mortality</td>
<td>13.752%</td>
</tr>
<tr>
<td>Morbidity or Mortality</td>
<td>43.654%</td>
</tr>
<tr>
<td>Long Length of Stay</td>
<td>33.454%</td>
</tr>
<tr>
<td>Short Length of Stay</td>
<td>4.79%</td>
</tr>
<tr>
<td>Permanent Stroke</td>
<td>7.595%</td>
</tr>
<tr>
<td>Prolonged Ventilation</td>
<td>34.567%</td>
</tr>
<tr>
<td>DSW Infection</td>
<td>0.514%</td>
</tr>
<tr>
<td>Renal Failure</td>
<td>15.7%</td>
</tr>
<tr>
<td>Reoperation</td>
<td>14.294%</td>
</tr>
</tbody>
</table>
Incremental Risk Factors

Frailty

Immobility – successful physical rehab?

Severe calcification of the aorta

Retrosternal grafts (previous bypass)

Chest radiation or chest wall deformity

Our 91 yo patient
Patient Selection

AS Severity
Symptoms

Surgical Risk Assessment
STS risk calculator
Incremental risk factors
Clinical judgment

“no stinkin’ calculator”
Current Categories Of Risk Status

**STS Risk:**
- Low: < 4%
- Intermediate: 4 to 8%
- High: > 8%

**Utility**

**Futility**
- Extreme: > 15%
Clinical Trial Data
“Extreme Risk” Patients, N ~ 800

TAVR

Reduction
- all-cause death and CV death (20% vs 50%)
- hospitalization

Improvement
- HF
- QoL

Mean age ~80, ~50% women, NYHA class III/IV HF

Medical therapy

Increased
- stroke rate (5% vs 1%)
- vascular complications
- pacemaker implantation

Yakubov SJ et al. JACC 2015.
Clinical Trial Data
“High Risk” Patients, N ~ 1,500

TAVR

Reduction
- all-cause death
  (22% vs 27%)

Similar Improvement
- HF
- QoL
- hospitalization

Surgical AVR (SAVR)

Increased
- stroke & TIA
  (10% vs 5%)
- vascular complications
- Paravalvular leak (PVL)
- pacemaker implantation (PPM)

Less bleeding and AFib

Mean age ~80, ~50% women, NYHA class III/IV HF

Reardon MJ et al. JACC 2014.
Clinical Trial Data
“Intermediate Risk” Patients, N ~2,000

Mean age ~80, ~50% women, NYHA class III/IV HF

TAVR

No difference
- mortality (17% vs 18.0%)
- disabling stroke (6.2% vs 6.4%)
- overall hospitalization
- re-intervention at 2 years

Benefit in TF-TAVR cohort

SAVR

Increased
- vascular complications (8% vs 6%)
- Paravalvular leak (PVL)
- Permanent pacemaker (PPM)

Less
- bleeding, kidney injury & AFib

Clinical Trial Data
“Low Risk” Patients

TAVR VS SAVR
TAVR-specific Risks and Complications

**Procedural**
- Vascular complications
- Cardiac perforation (tamponade)
- Device embolization

**Post Procedural**
- Paravalvular leak
- Heart block
- Leaflet thrombosis (?)

### 2014 AHA/ACC guideline for the management of patients with valvular heart disease

A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

*Developed in collaboration with the American Association for Thoracic Surgery, American Society of Echocardiography, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Anesthesiologists, and Society of Thoracic Surgeons*

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendation</th>
</tr>
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<tbody>
<tr>
<td>I</td>
<td>C</td>
<td>Evaluation by multidisciplinary Heart Team prior to intervention for severe valvular heart disease</td>
</tr>
<tr>
<td>I</td>
<td>A</td>
<td>Surgical AVR for patients at low or intermediate surgical risk</td>
</tr>
<tr>
<td>I</td>
<td>B</td>
<td>TAVR for patients with prohibitive surgical risk and prognosis &gt; 12 months</td>
</tr>
<tr>
<td>IIa</td>
<td>B</td>
<td>TAVR is a reasonable alternative to SAVR for patients with high surgical risk</td>
</tr>
<tr>
<td>IIb</td>
<td>C</td>
<td>Percutaneous BAV is reasonable as a bridge to TAVR or SAVR</td>
</tr>
<tr>
<td>III</td>
<td>B</td>
<td>TAVR should not be considered in patients with comorbidities expected to preclude benefit of correction of AS</td>
</tr>
</tbody>
</table>

Nishimura RA et al. JCTS. 2014.
Current Aortic Valve Therapy By Risk Status

STS Risk:
- Low < 4%
- Intermediate 4 to 8%
- High > 8%
- Extreme > 15%

Utility
- TAVR or SAVR

Futility
- TAVR
Future Directions

• Expanded indications:
  – Low risk patients?
  – Degenerative bioprosthetic aortic valves (“Valve-in-Valve”)
  – Severe aortic regurgitation
Future Directions

• Technological innovation:
  – Smaller profile delivery systems
  – Retrievable devices
  – Modifications to reduce PVL and CHB
  – Improved imaging guidance
The echocardiogram shows severe aortic stenosis. You recommend:

A. No further therapy because she is 91 years old
B. Surgical AVR
C. Transcatheter AVR (or TAVR)
D. Balloon aortic valvuloplasty
• You recommended, and she chose, TAVR.

• She had the implantation via transfemoral approach, had no post-procedural complications, and was discharged from hospital on day #3.

• 6 months later, she reports feeling “back to normal”.
IN CONCLUSION …

- The two biggest technological advances in interventional cardiology are bioabsorbable stents (BVS) and transcatheter aortic valve replacement (TAVR).

- Current clinical evidence suggests that BVS are comparable to DES in terms of clinical efficacy and safety – i.e. they are probably as safe and effective, but not more so.
  - We need, and are collecting, long-term data.

- Current clinical evidence suggests that TAVR may be superior to SAVR in extreme and high risk patients in terms of extending survival.
  - There are downsides to TAVR (vs. SAVR), including higher rate of stroke and prosthetic valve leak.
  - It is unclear whether TAVR is as good, better, or worse than SAVR with respect to lower risk patients.
THANK YOU FOR LISTENING!

ANY QUESTIONS?