Interventional Cardiology for the Non-Cardiologist: New Innovations and New Guidelines

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TOPICS
- Anti Platelet Therapy
- Updates on Bioresorbable Scaffolds
- Updates on TAVR
  (Transcatheter Aortic Valve Replacement)

Disclosures
No Conflicts of Interest

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Strength of Guideline Recommendations

Acronyms

- ACS: Acute Coronary Syndrome
- BMS: Bare Metal Stent
- CAD: Coronary Artery Disease
- CANG: Coronary Artery Bypass Graft Surgery
- DAPT: Dual Antiplatelet Therapy
- DES: Drug Eluting Stent
- PCI: Percutaneous Coronary Intervention
- PPI: Proton Pump Inhibitor
- SIHD: Stable Ischemic Heart Disease
- TAVR: Transcatheter Aortic Valve Replacement

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- Updates on TAVR
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Antiplatelet Agents

<table>
<thead>
<tr>
<th></th>
<th>Aspirin</th>
<th>Clopidogrel (Plavix)</th>
<th>Prasugrel (Effient)</th>
<th>Ticagrelor (Brilinta)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indication</td>
<td>ACS post PCI</td>
<td>ACS post PCI</td>
<td>Post PCI</td>
<td>ACS post PCI</td>
</tr>
<tr>
<td>Dose Load Maintenance</td>
<td>325 mg</td>
<td>300-600 mg</td>
<td>60 mg</td>
<td>180 mg</td>
</tr>
<tr>
<td>Class</td>
<td>NSAID</td>
<td>2nd gen</td>
<td>2nd gen</td>
<td>CTPT</td>
</tr>
<tr>
<td>Mechanism</td>
<td>IRREVERSIBLE</td>
<td>IRREVERSIBLE</td>
<td>IRREVERSIBLE</td>
<td>REVERSIBLE</td>
</tr>
<tr>
<td>Peak Effect</td>
<td>1-3 hours</td>
<td>6 hours</td>
<td>4 hours</td>
<td>2 hours</td>
</tr>
<tr>
<td>CYP Metab</td>
<td>NA</td>
<td>2C19</td>
<td>3A4</td>
<td>3A4/S</td>
</tr>
<tr>
<td>Hold prior to Surgery</td>
<td>?</td>
<td>5 days</td>
<td>7 days</td>
<td>5 days</td>
</tr>
</tbody>
</table>
Aspirin Dosing in Patients with Coronary Artery Disease (CAD)

Higher doses of aspirin are associated with bleeding and no increased anti-ischemic benefit
When used with ticagrelor (Brilinta), aspirin doses of >100 mg are contraindicated

According to US Guidelines, how long should patients be on Dual Antiplatelet Therapy (DAPT) after PCI with a Drug Eluting Stent?

A. 3 months  
B. 6 months  
C. 12 months  
D. It depends on the indication for PCI  
E. Call a cardiology consult

Duration of Dual Antiplatelet Therapy (DAPT)

- Duration of DAPT depends on:
  - Underlying condition
  - Treatment provided
Duration of Dual Antiplatelet Therapy (DAPT) in Patients with ACS

1 year
Stopping early at 6 months

Duration of Dual Antiplatelet Therapy (DAPT) in Patients with SIHD

Stable Ischemic Heart Disease (SIHD)

Stopping early at 3 months

When should DAPT therapy be continued for LONGER Duration?

Risk of Ischemia
- Increased risk of stent thrombosis
  - ACS presentation
  - Diabetes mellitus
  - Left ventricular ejection fraction < 40%
  - First-generation drug-eluting stent
  - Stent underdeployment
  - Small stent diameter
  - Greater stent length
  - Diffusion defects
  - In-stent restenosis

Risk of Bleeding
- Increased bleeding risk (may favor shorter-duration DAPT)
  - History of prior bleeding
  - Oral anticoagulant therapy
  - Female sex
  - Advanced age
  - Low body weight
  - CKD
  - Diabetes mellitus
  - Anemia
  - Chronic renal or NSAID therapy

The DAPT Score can guide risk / benefit of longer therapy

<table>
<thead>
<tr>
<th>Variable</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt; 75 y</td>
<td>-2</td>
</tr>
<tr>
<td>Age 65 to &lt;= 75 y</td>
<td>-1</td>
</tr>
<tr>
<td>Age &lt; 65 y</td>
<td>0</td>
</tr>
<tr>
<td>Current cigarette smoker</td>
<td>1</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1</td>
</tr>
<tr>
<td>MI at presentation</td>
<td>1</td>
</tr>
<tr>
<td>Prior PCI or prior MI</td>
<td>1</td>
</tr>
<tr>
<td>Stent diameter &lt; 3 mm</td>
<td>1</td>
</tr>
<tr>
<td>Paclitaxel-eluting stent</td>
<td>1</td>
</tr>
<tr>
<td>CHF or LVEF &lt; 30%</td>
<td>2</td>
</tr>
<tr>
<td>Saphenous vein graft PCI</td>
<td>2</td>
</tr>
</tbody>
</table>

Score ≥ 2 Favorable benefit/risk For prolonged DAPT

Score < 2 NOT Favorable benefit/risk For prolonged DAPT
Which P2Y12 Agent should I recommend?

<table>
<thead>
<tr>
<th>Condition</th>
<th>Ticagrelor (Brilinta)</th>
<th>Clopidogrel (Plavix)</th>
</tr>
</thead>
<tbody>
<tr>
<td>For Medically Managed ACS</td>
<td>Recommended over</td>
<td></td>
</tr>
<tr>
<td>For ACS with PCI</td>
<td>Recommended over</td>
<td></td>
</tr>
</tbody>
</table>

For patients with ACS, Ticagrelor is preferred for its rapid onset of action, while Clopidogrel is recommended for its long-term effectiveness.

What's the update on triple therapy?

- **For patients who require triple therapy:**
  - Use Coumadin (keep INR at low end of range)
  - Use Clopidogrel
  - Use low dose aspirin
  - Consider PPI

Perioperative Management and Timing of Non Cardiac Surgery

- Wait at least 3 months and preferably 6 months after PCI with DES
- Wait 30 days after PCI with BMS

65 yo man underwent PCI with a drug eluting stent to the LAD 2 months ago for stable angina. He now has severe knee osteoarthritis and is asking you when he can have surgery. How long after his stent should he wait?

- A. 1 month
- B. 3 months
- C. 6 months
- D. 12 months
- E. He should be managed medically indefinitely
Perioperative Management and Timing of Non Cardiac Surgery

**During perioperative period:**
- **Continue aspirin if possible**
- **Restart P2Y12 as soon as possible**

**Key Points Regarding DAPT (1/3)**
- Dose of Aspirin for all patients is **81 mg daily**
- Duration of DAPT:
  - ACS Patients: **1 YEAR for ALL** (with/without stent)
  - SIHD (Stable Ischemic Heart Disease) Patients:
    - Drug Eluting Stent (DES): **6 MONTHS**
    - Bare Metal Stent (BMS): **1 MONTH**
- Stopping Early:
  - DAPT could be stopped **3 months** after DES (drug eluting stent) for high bleeding risk patients
- Longer Therapy:
  - Risk benefit between bleeding and ischemia
  - DAPT score can be helpful

**Key Points Regarding DAPT (2/3)**
- Choice of Agents:
  - Medical Management of ACS: **Ticagrelor > Plavix**
  - PCI in ACS: **Ticagrelor or Prasugrel > Plavix**
  - **Do NOT USE Prasugrel** if history of stroke or TIA
- Triple Therapy:
  - Short Duration
  - Use clopidogrel/coumadin
  - Target INR 2-2.5
  - Use PPI (Proton Pump Inhibitor)

Class IIb (Level C)
Extrapolated from 2013 ACC/AHA STEMI Guidelines
Key Points Regarding DAPT (3/3)

- Timing of Non-Cardiac Surgery:
  - Ideally > 1 month after BMS, 6 months after DES
  - Continue Aspirin if possible
- Hold:
  - Clopidogrel 5 days prior to surgery
  - Ticagrelor 5 days prior to surgery
  - Prasugrel 7 days prior to surgery

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- Updates on TAVR (Transcatheter Aortic Valve Replacement)

Limitations of Current Metallic Stents

- The standard of care for PCI for the last decade has been metallic stents
  - Bare Metal or Drug Eluting
- Metallic stents have disadvantages:
  - Risk of stent thrombosis 0.1-0.2%/yr
  - Risk of repeat revascularization 2-3%/yr
  - Permanent implant cannot be removed

Bioresorbable Vascular Scaffold (BVS): ABSORB

- NO Permanent Implant!
  - Allows for restoration of vessel function (theoretical benefit)
  - Maintain option for future surgery (CABG)
  - Fewer permanent layers of metal in patients requiring treatment for stent restenosis (ISR)

ABSORB GT1 (Abbott Vascular)

Absorbable polymer, poly (L-lactide) (PLLA) with everolimus drug coating
A 52 yo M has ongoing CCS Class III stable angina despite maximal medical therapy. Coronary angiography demonstrates a 90% focal RCA lesion. He is considering PCI and requests your opinion regarding a bioresorbable stent. What do you tell him?

A. “It’s the latest and greatest, go for it”
B. “The risks and benefits appear to be similar to current metallic stents.”
C. “Steer Clear, at least for now!”

ABSORB III Trial: BVS comparable to DES

- 2008 patients with stable or unstable angina randomly assigned in a 2:1 ratio to receive Absorb or an everolimus-eluting cobalt–chromium (Xience) stent
- Primary end point: target lesion failure (cardiac death, target-vessel myocardial infarction, or ischemia-driven target-lesion revascularization) at 1 year

ABSORB III Results

- Target lesion failure non-inferior for ABSORB
- No difference in cardiac death at 1 (0.6% vs 0.1%, p=0.29)
-Signal for increase in stent thrombosis at 1 year (1.5% vs 0.7%, p=0.13)

Follow up data shows higher stent thrombosis (March 2017)

- AIDA trial showed significantly higher stent thrombosis
  27 events vs 5!
The fate of ABSORB

Results from 2 year follow up of ABSORB shown at American College of Cardiology Meeting (3/2017):

- Target Lesion Failure: 11.0% vs 7.9% (significant)
- Target Vessel Myocardial Infarction: 7.3% vs 4.9% (p=0.04)
- Stent Thrombosis: 1.9% vs 0.8%

Sales Halted September 2017

Key Points Regarding BVS

- Data through 2 years demonstrate a significantly higher risk of stent thrombosis with ABSORB bioresorbable vascular scaffold (BVS)
- FDA warning letter issued MARCH 2017
- ABSORB withdrawn from sale SEPTEMBER 2017

Bioresorbable Vascular Scaffolds May Not be Ready for Primetime

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An 82 yo lady presents to your office with severe shortness of breath while walking from her bed to the bathroom. She appears frail. On exam, you hear a 3/6 mid systolic murmur. She has 1+ LE edema at the shins. Echo shows severe aortic stenosis with LVEF 35%. What do you recommend?

A. Surgical Aortic Valve Replacement  
B. Transcatheter Aortic Valve Replacement  
C. Medical Therapy  
D. Hospice  
E. Ask my local cardiologist

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Aortic Stenosis

- Degree of Aortic Stenosis is determined by Echocardiography
- Symptoms are key!

AHA Guidelines for Severity of Aortic Stenosis

<table>
<thead>
<tr>
<th>Valve Area [(cm²)]</th>
<th>Maximum Aortic Velocity (mm/sec)</th>
<th>Mean Pressure Gradient (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>1.5-2</td>
<td>2.5-3.0</td>
</tr>
<tr>
<td>Moderate</td>
<td>1.0-1.5</td>
<td>3.0-4.0</td>
</tr>
<tr>
<td>Severe</td>
<td>0.6-1.0</td>
<td>&gt;4.0</td>
</tr>
<tr>
<td>Critical</td>
<td>&lt; 0.6</td>
<td></td>
</tr>
</tbody>
</table>

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2014 ACC/AHA Valvular Heart Disease (VHD) Guidelines

**Concept of Valve Disease Stages**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Definition</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>At risk</td>
<td>Patients with risk factors for the development of VHD</td>
</tr>
<tr>
<td>B</td>
<td>Progressive</td>
<td>Patients with progressive VHD (mild-to-moderate severity and asymptomatic)</td>
</tr>
<tr>
<td>C</td>
<td>Asymptomatic severe</td>
<td>Asymptomatic patients who have reached the criteria for severe VHD</td>
</tr>
</tbody>
</table>
|      |            | C1: Asymptomatic patients with severe VHD in whom the left or right ventricle remains compensated  
|      |            | C2: Asymptomatic patients who have severe VHD, with decompensation of the left or right ventricle |
| D     | Symptomatic severe | Patients who have developed symptoms as a result of VHD |

Valve replacement indicated for Stage C2 and D

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**Aortic Stenosis – Progression of Disease**

Intervening on patients with severe symptomatic AS improves survival
5 year survival of breast cancer, lung cancer, prostate cancer, ovarian cancer and severe inoperable aortic stenosis

**Survival Without Treatment is Poor**

![Graph showing 5-year survival rates for various cancers and severe aortic stenosis.](image)

**High Risk Patients Previously Untreated**

![Graph showing survival rates for high-risk patients.](image)

**TAVR Approved by FDA in US in 2011**

Multiple TAVR valve platforms have been developed

![Multiple TAVR valve platforms.](image)

**Two valves commercially available in US**

- **Edwards Sapien S3**
  - Bovine pericardial tissue
  - Stainless steel frame
  - Transfemoral, transapical, transaortic delivery
  - Balloon expandable system

- **Medtronic CoreValve**
  - Transfemoral or subclavian delivery
  - Repositionable, self-expanding system
Inoperable PARTNER Cohort
Primary Endpoint: All-Cause Mortality

Leon et al, NEJM 2010; 363:1597-1607

CoreValve US Pivotal Trial High Risk Study
3-Year Outcomes (Stroke)

KEY POINT:
For high risk and inoperable patients, TAVR is better than medical therapy and equivalent or better than surgery
TAVR has been studied across the risk spectrum of patients.

Two-thirds of patients are optimal surgical candidates.

- **Low Risk**
  - 30-Day Mortality < 2-4%
  - Surgical Aortic Valve Replacements: 70-90,000 yearly

- **Intermediate Risk**
  - 4-8%

- **High Risk**
  - ≥8%

- **Extreme Risk**
  - Top 4%

- **Futility**
  - Top 7%

- **Inoperable**
  - 20-50K

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- **Futility**
  - Top 7%

- **Inoperable**
  - 20-50K

Pivotal Trials for Intermediate Risk TAVR

- **SURTAVI Trial (NEJM 2017)**
  - TAVR with self expanding valve vs surgery (SAVR)
  - Intermediate Risk Patients (STS Score 4-8)
  - Severe Symptomatic Aortic Stenosis
  - Randomized Controlled Non-Inferiority Trial
  - Primary Endpoint: Composite of Death or disabling stroke at 24 months
  - 1746 patients randomized (1660 underwent valve replacement)
  - 87 centers
SURTAVI Trial (NEJM 2017) - Results

- Mortality similar (11.4 vs. 11.6%)
- Stroke numerically lower in TAVR (2.6% vs. 4.5%)

The tradeoff is higher rates of vascular complication and pacemaker implantation.

TAVR for Intermediate Risk Patients

KEY POINT:

For intermediate risk patients, TAVR is as effective as surgical repair, but has higher rates of pacemaker implantation and vascular injury.

What should a Primary Care Doctor know about TAVR patients?

2017 ACC Expert Consensus Decision Pathway for Transcatheter Aortic Valve Replacement in the Management of Adults With Aortic Stenosis

A Report of the American College of Cardiology Task Force on Clinical Expert Consensus Documents

Nichols, et al.
2017 ACC Focused Update of the 2014 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 Clinical Practice Guidelines
Point 1: Risk Evaluation Should Include STS Score (Risk of Mortality), Frailty and Comorbidities

- Low risk
  - STS-PROM - 4% or
  - No frailty and
  - No comorbidities and
  - No procedure-specific impediments
- Intermediate risk
  - STS-PROM 4%-8% or
  - Mild frailty or
  - 1 major organ system compromise not to be improved postoperatively or
  - 1 possible procedure-specific impediment
- High risk
  - STS-PROM - 8% or
  - Moderate severe frailty or
  - 2 major organ system complications not to be improved postoperatively or
  - 2 possible procedure-specific impediments
- Prohibitive risk
  - PROM >50% at 1 year or
  - 3 major organ system complications not to be improved postoperatively or
  - Severe frailty or
  - Severe procedure-specific impediments

STS - PROM = Predicted Risk of Mortality (30 Day)
Calculated at: http://riskcalc.sts.org/

Point 2: Intermediate risk patients are now indicated for TAVR (IIa)

Intermediate risk is indicated for TAVR.

Point 3: Long-Term Follow up for TAVR Patients Defined

- 6-8 Long-Term Follow-up
  - TAVR team at 30 days
  - Primary cardiologist at 6 months and then annually
  - Primary care MD or geriatrician at 3 months and then as needed
  - Antimicrobial therapy
    - ATRA 75 mg 50% of daily (oral)
    - Captopril 75 mg. daily for 3-6 months
    - Carotenoids (WAR 2.0.2.5) if at risk of AF or VTR
  - Concurrent cardiac disease
    - Coronary disease
    - Hyperlipidemia
    - Heart failure
    - Amyloidosis (especially AR)
    - Manage cardiac risk factors (including diet and physical activity)
  - Monitor for post-TAVR complications
    - Echocardiography at 30 days then annually (if normal)
    - ECG at 30 days and annually
    - Consider 24 h ECG in bradycondary
    - Encourage optimal dental care
    - Antibiotic prophylaxis per AHA/ACCI guidelines

Point 4: Endocarditis prophylaxis after TAVR

Patients with Transcatheter valves should receive endocarditis prophylaxis prior to dental procedures

- Infective Endocarditis (IE) has been reported to occur after TAVR at rates equal to or exceeding those associated with surgical aortic valve replacement (AVR)
- TAVR IE is associated with a high 1-year mortality rate of 75%
Point 5: Anticoagulation after TAVR

Anticoagulation with a VKA to achieve an INR of 2.5 may be reasonable for at least 3 months after TAVR in patients at low risk of bleeding.

- Studies have shown that valve thrombosis may develop in patients after TAVR, as assessed by CT scanning (7-40%).
- Valve thrombosis occurs in patients who received antiplatelet therapy alone but not in patients who were treated with VKA.

Point 6: Antiplatelet Therapy after TAVR

Clopidogrel 75 mg daily may be reasonable for the first 6 months after TAVR in addition to lifelong aspirin 75 mg to 100 mg daily.

Key Points Regarding TAVR (1/2)

- Risk assessment for patients should include STS Score, Frailty and Comorbidities.
- For Patients with Symptomatic Severe Aortic Stenosis (Stage D) whose risk for surgical valve replacement is:
  - **Inoperable**: TAVR has a **CLASS I** indication
  - **High Risk**: TAVR has a **CLASS I** indication
  - **Intermediate Risk**: TAVR is reasonable (**CLASS IIa**)
    - Risks for pacemaker placement are high
    - Risk for vascular complications remain elevated
  - **Low Risk**: Surgery is Preferred

Key Points Regarding TAVR (2/2)

- Patients with a TAVR valve should receive prophylaxis for endocarditis (**CLASS IIa**).
- Anticoagulation with a VKA antagonist (Coumadin) may be reasonable for 3 months after TAVR to prevent valve thrombus (**Class IIb**).
- Clopidogrel 75 mg daily for 6 months and ASA 81 mg daily for life may be reasonable after TAVR (**Class IIb**).
What Have We Learned?

Dual Antiplatelet Therapy
- Duration of DAPT after ACS and PCI
- Choice of Antiplatelet Agents
- An Approach to Triple Therapy with Anticoagulation and DAPT
- Timing of Non Cardiac Surgery after PCI

BioResorbable Stents
- Bioresorbable Stents are not ready for primetime!

Transcatheter Aortic Valve Replacement (TAVR)
- TAVR is now indicated for intermediate risk patients with Symptomatic Severe Aortic Stenosis
- Rates of pacemaker implantation and vascular injury are higher with TAVR compared to surgery
- Patients with TAVR valves should receive endocarditis prophylaxis
- Antiplatelet agents and VK antagonists may be considered for use after TAVR implantation

References

Guidelines


Trials
Thank You!

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