Updates in Interventional Cardiology and Guidelines

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Disclosures
No Conflicts of Interest

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TOPICS

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

Updates in Interventional Cardiology and Guidelines

- Major Society Guideline updates 2016-2017
- Clinical Trials Published 2016-2017
- Regulatory News and Events
Strength of Guideline Recommendations

TOPICS

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

Antiplatelet Agents

<table>
<thead>
<tr>
<th>Antiplatelet Agents</th>
<th>Aspirin (Plavix)</th>
<th>Clopidogrel (Plavix)</th>
<th>Prasugrel (Effient)</th>
<th>Ticagrelor (Brilinta)</th>
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<tbody>
<tr>
<td><strong>Indication</strong></td>
<td>ACS</td>
<td>Post PCI</td>
<td>Stroke</td>
<td>PVD</td>
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<tr>
<td><strong>Dose Maintenance</strong></td>
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<tr>
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<td>IRREVERSIBLE</td>
<td>REVERSIBLE</td>
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<tr>
<td><strong>Peak Effect</strong></td>
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<td>4 hours</td>
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<td>2C19</td>
<td>3A4</td>
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</table>
Aspirin Dosing in Patients with 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)

- PCI with Bare Metal Stent (BMS) 1 MONTH
- PCI with Drug Eluting Stent (DES) 6 MONTHS

Stopping early at 3 months

When should DAPT therapy be continued for LONGER Duration?

Risk of Ischemia
- Increased risk of stent thrombosis
  - Diabetes mellitus
  - Age ≥ 75 y
  - Age 65 to <75 y
  - Advanced age
  - Diabetes mellitus
  - Left ventricular ejection fraction <40%
  - First generation drug-eluting stent

Risk of Bleeding
- Increased bleeding risk (may favor shorter-duration DAPT)
  - History of prior bleeding
  - Female sex
  - Low body weight
  - CAD
  - Diabetes mellitus
  - Age
  - Chronic arterial or NOG therapy

The DAPT Score can guide risk/benefit of longer therapy

Score ≥ 2
- Favorable benefit/risk
- For prolonged DAPT

Score <2 NOT
- Favorable benefit/risk
- For prolonged DAPT

Which P2Y12 Agent should I recommend?

- For Medically Managed ACS
  - Recommended over
- For ACS with PCI
  - Recommended over

In patients with ACS (STEMI or NSTEMI) treated with DAPT after coronary stent implantation and in patients with NSTE ACS treated with medical therapy (for whom clopidogrel is standard), it is reasonable to use clopidogrel in preference to ticagrelor for maintenance P2Y12 inhibitor therapy (VIII.C.2.B).

In patients with ACS (STEMI or NSTEMI) treated with DAPT after coronary stent implantation who are not at high risk for bleeding complications and who do not have a history of stroke or TIAs, it is reasonable to choose prolonged over clopidogrel for maintenance P2Y12 inhibitor therapy (VIII.D.1).
**What's the update on 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**

**65 yo man underwent PCI with a drug eluting stent to the LAD 2 months ago for unstable 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
Key Points Regarding DAPT (1/2)

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

Key Points Regarding DAPT (2/2)

- 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
- Timing of Non-Cardiac Surgery:
  - Ideally > 1 month after BMS, 6 months after DES
  - **Continue Aspirin** if possible

TOPICS

- Anti Platelet Therapy
- Updates on Bioresorbable Scaffolds
- 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 scaffolds have **disadvantages**:
  - Rigid metallic cages hamper vasomotion
  - Development of neoatherosclerosis
    - Risk of stent thrombosis 0.1-0.2%/yr
    - Risk of repeat revascularization 2-3%/yr
  - Delayed stent endothelialization
  - 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)
- Thin coating of the absorbable polymer poly(D,L-lactide) (PDLLA) 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)

**FDA APPROVED July 2016**
Follow up data shows higher Stent Thrombosis (March 2017)

AIDA Trial

- 1845 patients undergoing PCI randomly assigned to receive either a bioresorbable vascular scaffold or a metallic stent.
- Primary end point: Target-vessel failure (a composite of cardiac death, target-vessel myocardial infarction, or target-vessel revascularization) through 2 years.
- The data and safety monitoring board recommended early reporting of the study results because of safety concerns.

AIDA Results – Target Lesion Failure

- Target lesion failure non-inferior for ABSORB

AIDA Results – Stent Thrombosis

- Definite Stent Thrombosis significantly higher for BVS
  - 27 events vs 5

The fate of ABSORB

FDA Warning Letter Issued March 2017

Results from 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%
The fate of ABSORB

- Removed from Commercial Use in the European Market
  (Registry only use allowed)

Key Points Regarding BVS

- Data through 2 years demonstrate a significantly higher risk of stent thrombosis with ABSORB
- FDA warning letter issued 3/2017
- ABSORB removed from commercial use in the EU (3/2017)

Bioresorbable Vascular Scaffolds May Not be Ready for Primetime

Updates in Interventional Cardiology and Guidelines

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

Aortic Stenosis

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

<table>
<thead>
<tr>
<th>AHA Guidelines for Severity of Aortic Stenosis</th>
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<tbody>
<tr>
<td>Valve Area (cm²)</td>
</tr>
<tr>
<td>------------------</td>
</tr>
<tr>
<td>Mild</td>
</tr>
<tr>
<td>Moderate</td>
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<tr>
<td>Severe</td>
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<tr>
<td>Critical</td>
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Valve replacement indicated for Stage C2 and D Aortic Stenosis – Progression of Disease

Intervening on patients with severe symptomatic AS improves survival

Survival Without Treatment is Poor

High Risk Patients Previously Untreated
TAVR Approved by FDA in US in 2011

Multiple TAVR Valve Platforms have been developed

- Direct Flow
- Lotus
- Acculink
- Avaulta
- Evolute
- Edwards Sapien

Bovine pericardial tissue
Stainless steel frame
PET skirt

Two valves commercially available in US

Edwards Sapien S3
- Transfemoral, transpical, transaortic delivery
- Balloon expandable system

Medtronic CoreValve
- Transfemoral or subclavian delivery
- Repositionable, self-expanding system

Inoperable PARTNER Cohort

Primary Endpoint: All-Cause Mortality

- Standard Rx
- TAVR

∆ at 1 yr = 20.0%
NNT = 5.0 pts
50.7%
30.7%

HR [95% CI] = 0.54 [0.38, 0.78]
P (log rank) < 0.0001

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

Primary Endpoint: All-Cause Mortality at 1 Year

HR [95% CI] = 0.93 [0.71, 1.22]
P (log rank) = 0.62
CoreValve US Pivotal Trial High Risk Study
3-Year Outcomes (All Cause Mortality)

- Lower all cause mortality for TAVR group

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

- Lower stroke for TAVR group

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

- Higher valve area and lower gradients for TAVR

TAVR for High Risk and Inoperable Patients

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:

- **Low Risk**
  - STS PROM < 4%
  - 30-Day Mortality < 2-4%

- **Intermediate Risk**
  - STS 4-8

- **High Risk**
  - STS > 8

- **Inoperable**

- **Extremely High Risk**

- **Cohort C**

- Two-thirds of patients will remain optimal surgical candidates.

Surgical Aortic Valve Replacements:

- 70-90,000 annually
- 20-50K inoperable

**Low Risk**
- STS PROM < 4%
- 30-Day Mortality < 2-4%

**Intermediate Risk**
- STS 4-8
- PARTNER IIA
- SURTAVI
- STS ≥ 4

**High Risk**
- PARTNER B
- CoreValve
- Extreme Risk
- Futility

TAVR has been studied across the risk spectrum of patients:

- 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)**

**Pivotal Trials for Intermediate Risk TAVR**

- Transcatheter or Surgical Aortic-Valve Replacement in Intermediate-Risk Patients

**SURTAVI Trial (NEJM 2017) - Results**

- **Primary outcome met!**
- **Death/Stroke at 24 months:** 12.6% vs 14%

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

As with other TAVR studies:
- Valve area is larger
- Valve gradients are lower

The Tradeoff is higher rates of vascular complication and pacemaker implantation
Point 1: Risk Evaluation Should Include STS Score, Frailty and Comorbidities

- Low risk: STS-PROM ≤ 4% and
- No frailty and
- No comorbidity and
- No procedure-specific impediments

- Intermediate risk: STS-PROM 4%-8% or
- Mild frailty or
- 1 MRS organ system compromise not to be improved postoperatively or
- A possible procedure-specific impediment

- High risk: STS-PROM ≥ 8% or
- Moderate-severe frailty or
- ≥2 MRS organ system complications not to be improved postoperatively or
- A possible procedure-specific impediment

- Prohibitive risk: STS-PROM > 50% at 1 year or
- ≥3 MRS organ system compromises not to be improved postoperatively or
- Severe frailty or
- Severe procedure-specific impediments

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

TAVR indicated for intermediate, high and prohibitive risk patients

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

- TAVR team at 30 days
- Primary cardiologist at 6 months and then annually
- Primary care MD or geriatrician at 5 months and then as needed

- Antithrombotic therapy: ASA 75 mg; 500 mg daily (if low)
- COUPLING 75 mg daily for 3-6 months
- Combined warfarin (INR 2.0-3.0) if at risk of AF or VTE

- Concurrent cardiac disease: Coronary disease
- Hypertension
- Heart failure
- Anemia (especially AR)
- Manage cardiac risk factors (including diet and physical activity)

- Monitor for post-TAVR complications:
  - Echocardiography at 30 days then annually (if needed)
  - ECG at 30 days and annually
  - Consider 24-h ECG if bradycardia

- Dental hygiene and antibiotics prophylaxis
  - Encourage optimal dental care
  - Antibiotic prophylaxis per AAP/ACE 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 life-long aspirin 75 mg to 100 mg daily.

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**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!

Transcatheater 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

Questions?
Thank You!

Questions / Final syllabus:
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