Understanding High-Risk Coronary and Peripheral Artery Disease (CAD/PAD) Patient Populations

July 15, 2020
Agenda

• What is CAD/PAD?
• What are the current guideline recommendations for CAD/PAD?
• Why the standard of care may not be enough
• What can we do better?
  • Risk assessment tools
  • Identification of high-risk patient populations
Overview of CAD/PAD
Atherosclerosis is a **CHRONIC** and **PROGRESSIVE** DISEASE\(^1,2\)

Inflammation + Hyperlipidemia + Diabetes + Hypertension + Stress + Smoking\(^3,4\)

Common Risk Factors of Atherosclerotic Cardiovascular Disease (ASCVD)¹-⁶

Nonmodifiable Risk Factors

- Age
- Family history
- Kidney function
- Sex
- Years since disease manifestation

Modifiable Risk Factors

- Blood pressure
- Cholesterol
- Type 2 diabetes
- Diet and exercise
- Weight/obesity
- Smoking status


This material is being presented by a healthcare professional in collaboration with the American Medical Group Association and is intended for providers involved in the care of patients with CAD and/or PAD.

Speaker is a paid consultant of Janssen Pharmaceuticals, Inc.
CV Disease Is a Potentially Deadly Condition Caused by Atherosclerosis, Often Manifesting as CAD or PAD\textsuperscript{1,2}

### Cardiovascular (CV) Disease

#### Atherosclerosis\textsuperscript{2}

Thickening and hardening of arteries from plaque restricts blood flow

### Peripheral Artery Disease (PAD)

Acute limb ischemia

Leg amputation

Revascularization

### Coronary Artery Disease (CAD)

Heart attack

Stroke/TIA

CV death

### CAD and PAD are associated with morbidity and mortality\textsuperscript{3-5}

TIA, transient ischemic attack.


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Strokes Subtypes\textsuperscript{1,2}


- **Cryptogenic**: 30%
- **Atherosclerotic Cerebrovascular Disease**: 20%
- **Hemorrhagic**: 13%
- **Cardioembolic**: 20%
- **Penetrating Artery Disease (Lacunes)**: 25%
- **Ischemic**: 87%
- **Other/Unusual Causes**: 5%
Revascularization and Amputation Rates in PAD Patients VARY BY GEOGRAPHY

Amputation Rates*

Revascularization Rates†

*Based on in-patient Medicare data from 2007-2009 (per 10,000 Medicare patients).
†Based on Medicare data from 2003-2006 in year prior to amputation for PAD.
High Mortality Rates Associated With Amputation

Risk of death nearly doubled with amputation

Time From Index Procedure to Death

- PAD With Amputation (n=186,338) 70.9%
- PAD Without Amputation (n=2,544,404) 43.2%

ALL-CAUSE MORTALITY RATE, %

Incidence/Prevalence of CAD and PAD

CV diseases are the leading cause of death in the United States and accounted for More than 850,000 deaths in 2017.1


CAD occurs in the vessels that feed the heart.2,3

18.2 million Americans ≥20 years of age had CAD in 2016.1

PAD occurs in other blood vessels in the body—most often in the legs but also in the brain, arms, and abdomen.4,5

8.5 million Americans ≥40 years of age had PAD in 2000.1

CAD, coronary artery disease; CV, cardiovascular; PAD, peripheral artery disease.

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**Escalating Cost of Atherosclerotic Disease in the United States**

Medical Cost of Atherosclerotic Disease in 2015 was **$318 Billion**

= 10% of Health Expenditures (2014)\(^1\)

| CAD\(^1\) | In 2015, cost of coronary heart disease was **$188 billion**
By 2035, costs are projected to **nearly double** |
| CVD\(^1\) | In 2015, cost of stroke was **$66 billion**
By 2035, costs are projected to **more than double** |
| PAD\(^2,3\) | Annual US total costs exceed **$21 billion**
Estimated **$10.6 billion** for amputations |

Polling Question

Who holds the primary responsibility for the management of these patients?

☐ Cardiologist
☐ Vascular Surgeon/Physician
☐ PCP
☐ More than 1 of the above
Current Standards of Care
**ACC/AHA Guidelines**

### Level 1A Recommendations on Antithrombotic Therapy for Patients With CAD or PAD

| CAD | **Acute treatment:** DAPT up to 12 months<sup>1,2</sup> |
| Symptomatic PAD | **Chronic treatment (>12 months): aspirin monotherapy<sup>1-3</sup>** |

**Aspirin monotherapy or clopidogrel<sup>1,4</sup>**

**Additional recommendations on secondary prevention and risk reduction therapy in these patients include smoking cessation, BP control, lipid management, physical activity, weight management, T2D management, RAAS blockers, beta-blockers, influenza vaccination, treatment of depression, and cardiac rehabilitation.**

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ACC, American College of Cardiology; AHA, American Heart Association; BP, blood pressure; CAD, coronary artery disease; DAPT, dual antiplatelet therapy; PAD, peripheral artery disease; PCI, percutaneous coronary intervention; RAAS, renin-angiotensin-aldosterone system; T2D, type 2 diabetes.

<sup>1</sup>A P2Y<sub>12</sub> receptor antagonist in combination with aspirin after acute coronary syndrome or PCI with stent placement.<sup>1</sup>


<sup>4</sup>Fihn SD et al. *J Am Coll Cardiol.* 2012;60(24):e44-e164.
2019 Guidelines Recommend Individualized Antithrombotic Therapy According to Individual Risk of Ischemia

2019 ESC Guidelines for the Diagnosis and Management of Chronic Coronary Syndromes

**Recommendations**

Antithrombotic therapy in patients with CCS and in sinus rhythm

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Class</th>
<th>Evidence level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adding a <strong>second antithrombotic drug</strong> to aspirin for long-term secondary prevention should be considered in patients with a <strong>high risk of ischemic events</strong> and without high bleeding risk*</td>
<td>IIa</td>
<td>A</td>
</tr>
<tr>
<td>Adding a <strong>secondary antithrombotic drug</strong> to aspirin for long-term secondary prevention may be considered in patients with at least a <strong>moderately increased risk of ischemic events</strong> and without high bleeding risk*</td>
<td>IIb</td>
<td>A</td>
</tr>
</tbody>
</table>

*High bleeding risk is defined as prior history of intracerebral hemorrhage or ischemic stroke, history of other intracranial pathology, recent gastrointestinal bleeding or anemia due to possible gastrointestinal blood loss, other gastrointestinal pathology associated with increased bleeding risk, liver failure, bleeding diathesis or coagulopathy, extreme old age or frailty, or renal failure requiring dialysis or with eGFR <15 mL/min/1.73m².

**High ischemic risk defined as diffuse multivessel CAD with at least 1 of the following:**
- Diabetes mellitus requiring medication
- Recurrent MI
- PAD
- CKD with eGFR 15 to 59 mL/min/1.73m²

**Moderate ischemic risk defined as at least 1 of the following:**
- Diabetes mellitus requiring medication
- Recurrent MI
- PAD
- Multivessel/diffuse CAD
- HF
- CKD with eGFR 15 to 59 mL/min/1.73m²

See the full 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes for all recommendations.
Polling Question

Were you aware there are updated therapy guidelines that recommend evaluating high-risk patients for individualized therapy?

☐ Yes
☐ No
Opportunities for Improvement in Standards of Care
Undertreatment in PAD Is Common

Nonuse of Recommended Therapies*

- Statin: 81.7%
- ACE-I/ARB: 79.2%
- Any Antiplatelet Therapy: 72.6%

*Data are from 1999-2004.
†PAD patients without CV disease (defined as MI, angina, coronary heart disease, or stroke).
Undertreatment of CAD Patients Is Common

1 in 3 (33.5%) of Eligible CAD Patients Were NOT Prescribed Guideline-Based Therapy With Antiplatelet, Beta-Blocker, ACE-I/ARB, and Statin*

*Data are from 2008-2010.
ACE-I angiotensin converting enzyme inhibitor; ARB, angiotensin II receptor blocker
In the REACH Registry following patients with CAD/PAD, MAJOR CARDIOVASCULAR EVENT RATES DOUBLED even with high use of standard medications and treatments\(^1\)

Major cardiovascular event rates at 1 and 3 years\(^*\)

\[^*\] In patients with symptomatic disease, major cardiovascular events (defined as MI; stroke; cardiovascular death; rehospitalization for a vascular event other than cardiovascular death, MI, or stroke) in patients eligible for 1-year (n=53,211) and 3-year (n=39,675) evaluations. Patient enrollment began in December 2003 and ended in December 2004.

Patients With Chronic CAD/PAD in REACH Remained at Residual Risk of CV Events

Risk of CV death, MI, or stroke at 4 years

Most clinical events result from unstable plaques; however, patients with stable disease are also at risk.

Patients with atherosclerosis with a prior ischemic event* 18.3%

Patients with stable disease without prior ischemic events 12.2%

CV Risk Factors
- Hypertension
- Hypercholesterolemia
- Diabetes

- Obesity (BMI ≥30)
- Smoker
- Heart failure
- Atrial fibrillation

CV, cardiovascular; BMI, body mass index; MI, myocardial infarction; REACH indicates REduction of Atherothrombosis for Continued Health.

*Prior ischemic event is defined as MI or stroke.

Bhatt DL et al; REACH Registry Investigators. JAMA. 2010;304(12):1350-1357.
Strategies for Improved Patient Care
Vascular Protection Requires a Combination of Antithrombotic and Risk Factor Management¹,²

VASCULAR PROTECTION

VASCULAR PREVENTION

Antithrombotic Therapy

RISK FACTOR CONTROL

Lifestyle Modification and Additional Drug Therapy

Lifestyle Modifications for SECONDARY CV EVENT PREVENTION

2011 AHA/ACC and 2019 ESC guidelines recommend lifestyle modifications for the secondary prevention and reduction in the risk of CV events in patients with CAD and PAD and other atherosclerotic vascular disease.1,2

Smoking cessation
Healthy diet
Physical activity
Weight management
Medication adherence

Please consult the full 2019 ESC and 2011 AHA/ACC Guidelines for all recommendations.

ACC, American College of Cardiology; AHA, American Heart Association; CAD, coronary artery disease; CV, cardiovascular; ESC, European Society of Cardiology; PAD, peripheral artery disease.
Pharmacologic Treatment Is Recommended for Patients With CAD and PAD

Current AHA/ACC guidelines recommend pharmacologic treatments for the secondary prevention and reduction in the risk of CV events in patients with CAD and PAD.

<table>
<thead>
<tr>
<th>Blood Pressure Control</th>
<th>Goal</th>
<th>Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>BP &lt;140/90 mm Hg</td>
<td></td>
<td>Initial treatment with β-blockers and/or ACE inhibitors, with addition of other drugs as needed</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Lipid Management</th>
<th>Goal</th>
<th>Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDL &lt;100 mg/dL</td>
<td></td>
<td>Statin therapy in the absence of contraindications or documented adverse effects</td>
</tr>
<tr>
<td>Non-HDL &lt;130 mg/dL</td>
<td></td>
<td>If triglycerides are ≥200 mg/dL, statin therapy to lower non-HDL to &lt;130 mg/dL</td>
</tr>
<tr>
<td>VERY HIGH-RISK PATIENTS:</td>
<td>LDL &lt;70 mg/dL</td>
<td>If triglycerides are &gt;500 mg/dL, fibrate therapy in addition to statin therapy</td>
</tr>
<tr>
<td></td>
<td>Non-HDL &lt;100 mg/dL</td>
<td></td>
</tr>
<tr>
<td></td>
<td>If triglycerides are ≥200 mg/dL, Non-HDL &lt;130 mg/dL</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Antithrombotic Therapy</th>
<th>Goal</th>
<th>Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>N/A</td>
<td></td>
<td>Aspirin 75-325 mg daily or clopidogrel 75 mg daily</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Type 2 Diabetes Management</th>
<th>Goal</th>
<th>Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c ≤7%</td>
<td></td>
<td>Initiate pharmacotherapy to achieve target HbA1c Metformin as first-line pharmacotherapy, if not contraindicated</td>
</tr>
</tbody>
</table>

Please consult the full AHA/ACC Guidelines for all recommendations

ACC, American College of Cardiology; ACE, angiotensin-converting enzyme; AHA, American Heart Association; BP, blood pressure; CAD, coronary artery disease; CV, cardiovascular; HbA1c, glycated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; N/A, not applicable; PAD, peripheral artery disease.

*A less stringent HbA1c goal may be considered in certain patients (e.g., those with a history of severe hypoglycemia, limited life expectancy, advanced vascular complications, or extensive comorbidities, or those who are unable to attain goal HbA1c despite intensive therapy). Smith SC Jr et al; World Heart Federation and the Preventive Cardiovascular Nurses Association. Circulation. 2011;124(22):2458-2473.
Risk assessment tools have been generally based on the Framingham Risk Score and the pooled cohort equations.

Both have been shown to overestimate and underestimate risk in some individuals. Additional tests (for nontraditional risk factors) that could improve risk prediction need to be identified.

Accurate identification of patients at high risk enables more intensive risk factor management to reduce the chance of a CV event.

Risk estimation in patients with CVD can help support decision-making for targeted secondary prevention of CV events.

CV, cardiovascular; CVD, cardiovascular disease.
ACC ASCVD Primary Prevention Risk Evaluator Plus Tool

### ACC ASCVD Primary Prevention Risk Evaluator Plus Tool

**App should be used for primary prevention patients (those without ASCVD) only.**

<table>
<thead>
<tr>
<th>Current Age</th>
<th>Sex</th>
<th>Race</th>
</tr>
</thead>
<tbody>
<tr>
<td>App must be between 18-90</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: These estimates only underestimate the 10-year and lifetime risk for patients from some racial/ethnic groups, especially American Indians, some Asian Americans (e.g., of south Asian ancestry), and some Hispanics (e.g., Puerto Ricans), and may overestimate the risk for others, including some Asian Americans (e.g., of east Asian ancestry) and some Hispanics (e.g., Mexican Americans). Because the primary use of these risk estimates is to facilitate the very important discussion regarding risk reduction through lifestyle change, the imprecision introduced is small enough to justify proceeding with lifestyle change counseling informed by these results.

- **Systolic Blood Pressure (mm Hg)**
  - Value must be between 90-200

- **Diastolic Blood Pressure (mm Hg)**
  - Value must be between 50-90

- **Total Cholesterol (mg/dL)**
  - Value must be between 100-500

- **HDL Cholesterol (mg/dL)**
  - Value must be between 50-150

- **LDL Cholesterol (mg/dL)**
  - Value must be between 30-150

- **History of Diabetes?**

- **Smoker?**

- **How long ago did patient quit smoking?**

- **On Hypertension Treatment?**

- **On a Statin?**

- **On Aspirin Therapy?**

**Do you want to refine current risk estimation using data from a previous visit?**

### Risk Categories

- **Low Risk**
  
  
  
  - <5.0%

- **Borderline Risk**
  
  
  
  - 5.0% - 7.4%

- **Intermediate Risk**
  
  
  
  - 7.5% - 19.9%

- **High Risk**
  
  
  
  - ≥20.0%

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ACC, American College of Cardiology; ASCVD, atherosclerotic cardiovascular disease. *App is intended for primary prevention for patients without ASCVD.


Estimates individual 10-year ASCVD risk at initial visit*

Assumes no previous cardiovascular disease

Forecasts potential impact of interventions on patient risk

Aids clinician-patient discussions on risk and risk-lowering interventions

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SMART Assessment Tools

SMART Risk Score

Estimates individual 10-year risk for MI, stroke, or vascular death in patients with previous CVD (including CAD and PAD) if standard care is provided. Developed through an analysis of a secondary prevention population of patients with vascular disease (N = 6904) from the SMART study.

The results of this analysis indicated that:
- A total of 18% of patients had a <10% risk of recurrent CV event at 10 years; 22% had a >30% risk at 10 years
- If all modifiable risk factors were at guideline-recommended targets, 10-year risk of recurrent vascular events could be reduced to <10% for about half of the patients with vascular disease; 20% remained at >20% risk and 9% remained at >30% risk of recurrent event

SMART–REACH Model

Estimates 10-year CV event risk and improvement in life expectancy without recurrent CV events in individuals with CAD and/or PAD, if preventive treatment is provided.

ACC/AHA Very High-Risk Criteria

**REACH Cohort**

- **MACE:** 2773 events
- Average incidence of recurrent MACE: 5.1/100 PY
- Median follow-up: 1.8 years

**SMART Cohort**

- **MACE:** 1185 events
- Average incidence of recurrent MACE: 2.4/100 PY
- Median follow-up: 6.5 years

### Incidence for Recurrent MACE With Select High-Risk Factors

<table>
<thead>
<tr>
<th>Factor</th>
<th>REACH Registry</th>
<th>SMART Registry</th>
</tr>
</thead>
<tbody>
<tr>
<td>AAA or PAD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>eGFR &lt;45</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Polyvascular disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Progression of CAD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
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</tr>
</tbody>
</table>

**IR/100 PY**

- **REACH Registry**
- **SMART Registry**


AAA, abdominal aortic aneurysm; ACC, American College of Cardiology; AHA, American Heart Association; CAD, coronary artery disease; eGFR, estimated glomerular filtration rate; IR, incidence rate; MACE, major adverse cardiovascular events; PAD, peripheral artery disease; PY, person years; REACH, REduction of Atherothrombosis for Continued Health; SMART, Second MANifestations of ARTerial disease.
Which Patients Are at HIGHEST RISK For Ischemic Events?

<table>
<thead>
<tr>
<th>Diffuse Multivessel CAD (Polyvascular)*</th>
<th>PAD</th>
<th>Heart Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal Insufficiency†</td>
<td>Recurrent MI</td>
<td>Diabetes‡</td>
</tr>
</tbody>
</table>

*≥2 vascular beds
†eGFR 15-59 mL/min.
‡Requires medication.

Polling Question

What will you do differently after this presentation?

☐ Create care pathway for CAD/PAD patients
☐ Apply patient identification at point of EHR
☐ Educate health system on CAD/PAD
☐ Nothing different
☐ Other

CAD, coronary artery disease; PAD, peripheral artery disease.
Overview of CAD and PAD

- Chronic CAD/PAD cost the US healthcare system billions of dollars a year and these patients are at risk of secondary thrombotic events associated with ASCVD\(^1-6\)

Current Standards of Care

- Updated therapy guidelines recommend evaluating high-risk patients for individualized therapy\(^7\)

Opportunities for Improvement in Standards of Care

- Risk of CV events exists even for patients with stable disease\(^8\)

Strategies for Improved Patient Care

- Targeted risk assessment tools can help to accurately identify high-risk CAD/PAD patients who can benefit from more intensive risk factor management and follow up strategies\(^9\)

ASCVD, atherosclerotic cardiovascular disease; CAD, coronary artery disease; CV, cardiovascular; PAD, peripheral artery disease.