MHIF FEATURED STUDY: Vesalius

DESCRIPTION:
The purpose of this trial is to evaluate the effect Evolocumab has in reducing the risk of coronary heart disease (CHD) death, MI, stroke, and ischemia-driven arterial revascularization in adults at high risk of cardiovascular events without prior MI or stroke.

CRITERIA LIST/QUALIFICATIONS:

Inclusion
- ≥ 50 years (men); or ≥ 55 years (women) to < 80 years of age (either sex)
- LDL-C ≥ 100 mg/dL (≥ 2.6 mmol/L) or HDL-C ≥ 130 mg/dL (≥ 3.4 mmol/L) on maximal tolerated therapy
- CAD w revasc
- High calcium score (≥100)
- TIA, carotid revasc, PVD
- DM with microvascular disease
- PLUS one high risk criteria: polyvascular disease, metabolic syndrome, Lp(a)>125, LDL ≥130, known FH, fam hx premature CAD, CRP ≥3, current tobacco, ≥ 65 yrs, eGFR < 45
**MHIF FEATURED STUDY:**

**Lp(a)**

**DESCRIPTION:**
The purpose of this trial is to improve knowledge about the epidemiology of Lp(a) in pts with established CVD. Lp(a) is a lipoprotein in which the apo(B) component of LDL is linked to bond apo (a). Lp(a) is now recognized as an independent, genetic, causal risk factors for CAD, stroke, PAD and calcific aortic stenosis.

**CRITERIA LIST/ QUALIFICATIONS:**

<table>
<thead>
<tr>
<th>Inclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male and female ≥18 ≤ 80</td>
</tr>
<tr>
<td>Established CVD: Hx of MI or Hx of ischemic stroke or symptomatic PAD</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pts currently enrolled in clinical studies with investigational drugs</td>
</tr>
</tbody>
</table>

**CONDITION:** Established CVD

**PI:** Thomas Knickelbine, MD

**RESEARCH CONTACT:**
Steph Ebnet  
Stephanie.ebnet@allina.com |  
612-863-6286

**SPONSOR:** NOVARTIS

(Almost) OPEN AND ENROLLING: Please Refer Patients!
Title: Spontaneous Coronary Artery Dissection: Unraveling an Enigma

Speakers: Christina Thaler, MD, PhD
Cardiovascular Disease Fellow
Minneapolis Heart Institute® at Abbott Northwestern Hospital &
Hennepin Healthcare

Date: December 2, 2019
Time: 7:00 – 8:00 AM
Location: Minneapolis Heart Institute Building, Suite 100, Learning Center

OBJECTIVES
At the completion of this activity, the participants should be able to:
1. Identify the challenges of diagnosing SCAD.
2. Review the evidence for acute and long term management of SCAD.
3. Characterize the complications associated with SCAD.

DISCLOSURE POLICY & STATEMENTS
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Moderator(s)/Speaker(s)
Dr. Christina Thaler has disclosed that she DOES NOT have any real or apparent conflicts with any commercial interest as it relates to presenting the content in this activity/course.

Planning Committee
Dr. Alex Campbell, Jake Cohen, Jane Fox, Dr. Kevin Harris, Dr. Kasia Hryniewicz, Rebecca Lindberg, Amy McMeans, Dr. Michael Miedema, Dr. JoEllyn Moore, Pamela Morley, Dr. Scott Sharkey, Maia Hendel and Jolene Bell Makowesky have disclosed that they DO NOT have any real or apparent conflicts with any commercial interest as it relates to the planning of this activity/course. Dr. Mario Gössl has disclosed the following relationships – Edwards Life Sciences: Grant/Research Support; Abbott Vascular, Caisson: Consultant; Speaker’s Bureau: Edwards Lifesciences. Dr. David Hurrell has disclosed the following relationship –Boston Scientific: Chair, Clinical Events Committee.

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Unraveling an Enigma: Spontaneous Coronary Artery Dissection

DECEMBER 2, 2019

CHRISTINA THALER, MD PHD
CARDIOLOGY FELLOW
MINNEAPOLIS HEART INSTITUTE
HENNEPIN COUNTY MEDICAL CENTER

Conflicts of Interest

► No conflicts of interest

► SCAD Research funded in part by MHI Foundation Grant

► Acknowledgements - SCAD Research
  ► Scott Sharkey, MD
  ► Betty Grey, MD
  ► Tim Henry, MD
  ► Meagan Nowariak
Case: 55 year old woman with chest pain

- Sudden onset of severe sharp mid chest pain radiating to her left arm
- Past Medical History: None
- Vitals: BP 160/90, P 63, T 36.1C, SpO2 97%
- Exam: Unremarkable
- Labs: BMP, CBC normal, Troponin negative
- Given aspirin, SL Nitroglycerin, morphine, and heparin
- Admitted for Chest Pain Rule Out, Chest pain never resolved

Next Morning ...

- Troponin positive at 0.19 mcg/L
- Transferred to Abbott Northwestern with ongoing chest pain
- Received PCI to 1st Obtuse Marginal
Ongoing Chest Pain ...

- Delayed Gadolinium Enhancement
- T2: STIR

- Question of Embolic Process for Inferior MI
- Bilateral Lower Extremity DVT US Negative
- Hypercoagulability Work-up Negative
- Standard Treatment for Atherosclerotic Coronary Artery Disease
- Cardiac Rehab Recommended a Home Exercise Program

Continued Chest Pain 5 days later

- New 50% lesion in LAD noted, but not considered to be significant
- Discharged home with diagnosis obstructive and embolic coronary artery disease
Outpatient Follow-up

- Continued to have severe anginal chest pain
- Angiogram 3 months later with resolution of prior LAD lesion
- Diagnosed with vasospasm
- Started on ranolazine, amlodipine added later
- Treated with antidepressant for depression and anxiety
- 3 years later, recurrent chest pain with negative troponins and stable angiogram

Repeat Chest Pain 9 Years Later

- Troponin positive 0.1 mcg/L, EKG unremarkable
- Received standard treatment for NSTEMI
- SCAD of LAD with evidence of fibromuscular dysplasia on femoral angiogram
- Restarted on a beta blocker for treatment of recurrent SCAD
SCAD with Fibromuscular Dysplasia: A Unifying Diagnosis

Outline

- Diagnosis
- Acute Management
- Long term management / follow-up
What is SCAD?

- Separation of coronary artery intima from media (dissection) by hematoma resulting in coronary lumen obstruction

Hematoma Progression

- Longitudinal extension
- Axial compression
- Decompression with secondary intimal tear
- Early improvement + resolution

Demographics

Table I  Demographics and risk factors of patients with spontaneous coronary artery dissection (SCAD) in contemporary case series (studies with n > 20)

<table>
<thead>
<tr>
<th>Study</th>
<th>Max N</th>
<th>Age (years)</th>
<th>Gender (female, %)</th>
<th>HTN (%)</th>
<th>Chol (%)</th>
<th>Smoking (%)</th>
<th>DM (%)</th>
<th>FH (%)</th>
<th>P-SCAD (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mayo Clinic</td>
<td>189</td>
<td>44 ± 9</td>
<td>93</td>
<td>31</td>
<td>22</td>
<td>15</td>
<td>2</td>
<td>NA</td>
<td>15</td>
</tr>
<tr>
<td>Saw1</td>
<td>168</td>
<td>52 ± 9</td>
<td>93</td>
<td>39</td>
<td>24</td>
<td>13</td>
<td>5</td>
<td>29</td>
<td>2</td>
</tr>
<tr>
<td>Listeri1</td>
<td>134</td>
<td>52 ± 11</td>
<td>81</td>
<td>51</td>
<td>33</td>
<td>34</td>
<td>2</td>
<td>25</td>
<td>NA</td>
</tr>
<tr>
<td>Faden6</td>
<td>79</td>
<td>33 ± 5</td>
<td>100</td>
<td>17</td>
<td>18</td>
<td>17</td>
<td>11</td>
<td>NA</td>
<td>100</td>
</tr>
<tr>
<td>Rogowsk6</td>
<td>64</td>
<td>53 ± 11</td>
<td>94</td>
<td>45</td>
<td>52</td>
<td>28</td>
<td>0</td>
<td>19</td>
<td>5</td>
</tr>
<tr>
<td>Nakashima8</td>
<td>63</td>
<td>46 ± 10</td>
<td>94</td>
<td>33</td>
<td>23</td>
<td>32</td>
<td>0</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>McMurtry-Cadel8</td>
<td>40</td>
<td>45 ± 10</td>
<td>95</td>
<td>18</td>
<td>10</td>
<td>8</td>
<td>5</td>
<td>28</td>
<td>8</td>
</tr>
<tr>
<td>Rora10</td>
<td>34</td>
<td>47 ± 12</td>
<td>94</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>15</td>
</tr>
<tr>
<td>Alkonsos11</td>
<td>27</td>
<td>52 ± 10</td>
<td>85</td>
<td>37</td>
<td>33</td>
<td>52</td>
<td>4</td>
<td>NA</td>
<td>4</td>
</tr>
<tr>
<td>Re12</td>
<td>23</td>
<td>45 ± 11</td>
<td>100</td>
<td>57</td>
<td>22</td>
<td>30</td>
<td>4</td>
<td>NA</td>
<td>30</td>
</tr>
<tr>
<td>Vannotti14</td>
<td>21</td>
<td>46 ± 9</td>
<td>74</td>
<td>26</td>
<td>39</td>
<td>43</td>
<td>13</td>
<td>13</td>
<td>0</td>
</tr>
<tr>
<td>Mortazawian15</td>
<td>22</td>
<td>49 ± 9</td>
<td>81</td>
<td>38</td>
<td>NA</td>
<td>57</td>
<td>0</td>
<td>40</td>
<td>10</td>
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<tr>
<td>Rashid16</td>
<td>21</td>
<td>53 ± 9</td>
<td>95</td>
<td>48</td>
<td>48</td>
<td>47</td>
<td>5</td>
<td>24</td>
<td>0</td>
</tr>
</tbody>
</table>


Age Distribution

- 90% less than 65 years

[Saw J Am Coll Cardiol 2017;70:1148–58]
SCAD Presentation

- Peripartum: < 5%
- Normal ECG: 20%
- Emotional stress: 50%
- Heavy isometric exercise: 10%

Diagnosis by Angiogram

Type 1

Type 2

Type 3

Type 1 SCAD

LAD

[SAW J Am Coll Cardiol 2017;70:1148-58]
Type 2 SCAD LAD

Type 3 SCAD LAD
Type 3 SCAD
LAD

SCAD Multi-Vessel

Coronary Distribution

Multi-vessel: 14% (9% non-contiguous)
Multimodality Imaging Enhances SCAD Diagnosis

- Optical Coherence Tomography / Intravascular Ultrasound to confirm dissection
  - Improved spatial resolution
  - Only recommend if diagnosis is unclear due to dissection risk
- CT coronary angiography
  - Exclude significant atherosclerotic disease
  - Useful to visualize proximal dissections
- Cardiac MRI
  - Diagnose and confirm location of myocardial infarction

Spatial Resolution: Coronary Imaging Modalities

<table>
<thead>
<tr>
<th>Imaging Modality</th>
<th>Spatial Resolution</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT Coronary Angiography</td>
<td>300–400 μm</td>
</tr>
<tr>
<td>Invasive angiography</td>
<td>150–200 μm</td>
</tr>
<tr>
<td>Intra-vascular ultrasound</td>
<td>100–200 μm</td>
</tr>
<tr>
<td>Optical Coherence Tomography</td>
<td>15 μm</td>
</tr>
</tbody>
</table>

Cardiac CT Angiography


Cardiac MRI in Diagnosis of SCAD

- 60 year old woman without significant medical history had NSTEMI with troponin to 12
- Angiogram with "normal coronary arteries"
- cMRI transmural infraction of the basal to mid interventricular septum with wall motion abnormality
Diagnosis of SCAD

- Diagnosis can be challenging
- Coronary Angiography primary modality for diagnosis
- Multimodality Imaging can augment coronary angiography

Acute Management

Management of acute spontaneous coronary artery dissection (SCAD)

- Clinically stable, no high-risk anatomy
  - Conservative therapy
  - Monitor as inpatient 3-5 days
- Clinically stable with left main or severe proximal 2-vessel dissection
  - Consider CABG
  - Conservative Rx may be reasonable (not studied)
- Active/ongoing ischemia or hemodynamic instability
  - Consider PCI if feasible
  - OR
  - Urgent CABG (based on technical considerations and local expertise)

**SCAD Treatment Conservative**

- Spontaneous healing 70-90%
  - Predominantly NSTEMI
- Often healed by 1 month
- Repeat angiography only based on clinical symptoms


**SCAD Early Progression**

- 5-20% of patients will have early progression of disease
- 2.6-8.5% will fail conservative treatment
- Hospitalized minimum 48 hours, up to 5 days can be justified

*Figure 1. Timing of spontaneous coronary artery dissection (SCAD) progression.*

Risk Factors for Progression of SCAD

<table>
<thead>
<tr>
<th>Model variable</th>
<th>Estimate</th>
<th>Std Error</th>
<th>Odds ratio</th>
<th>Lower CL</th>
<th>Upper CL</th>
<th>Odds Ratio (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isolated IMH</td>
<td>1.25</td>
<td>0.41</td>
<td>3.49</td>
<td>1.57</td>
<td>7.78</td>
<td></td>
<td>0.002</td>
</tr>
<tr>
<td>Multi-vessel</td>
<td>1.21</td>
<td>0.48</td>
<td>3.35</td>
<td>1.29</td>
<td>8.66</td>
<td></td>
<td>0.01</td>
</tr>
<tr>
<td>Stenosis (&gt;80%)</td>
<td>0.92</td>
<td>0.44</td>
<td>2.50</td>
<td>1.06</td>
<td>5.89</td>
<td></td>
<td>0.04</td>
</tr>
<tr>
<td>Lesion Length (&gt;60 mm)</td>
<td>0.76</td>
<td>0.43</td>
<td>2.15</td>
<td>0.93</td>
<td>4.94</td>
<td></td>
<td>0.07</td>
</tr>
<tr>
<td>LAD</td>
<td>0.39</td>
<td>0.43</td>
<td>1.48</td>
<td>0.64</td>
<td>3.43</td>
<td></td>
<td>0.30</td>
</tr>
</tbody>
</table>


Progression in New Vessels During Index Admission
SCAD Revascularization

- Technically Challenging
- Technical failure: 25-36%
- Suboptimal results: 25%
- Emergency CABG 9-12%


MHI Experience with Revascularization

- 58 of 122 (48%) patients between 2004-2019 received revascularization
  - 54 Patients Received Angioplasty with Stenting
  - 1 Patient Received Angioplasty alone
  - 3 Patients Received Angioplasty with CABG
  - PCI with Stenting
    - Medium Stent Number: 2 (range 1-7)
    - Total PCI Length: 46mm (IQR 25, 82.5)
    - Drug Eluting Stents: 98%
  - Demographics
    - Median Age 47.8 years (range 20-90 years)
    - 56/59 (98%) Female
High Risk Features in Patients with Revascularization

- STEMI: 31 (53.5%)
- Cardiac Arrest: 9 (15.5%)
- Proximal Lesions: 38 (65.5%)
- Left Main: 8 (11.3%)
- Left Anterior Descending Artery: 37 (52.1%)
- Multi-vessel: 9 (15.5%)
- 33 (56.8%) TIMI 0 or 1 Flow

Outcomes: Median Follow Up 4.1 years (Range 0-13.9)

- Left Ventricular Ejection Fraction
  - > 55%: 46 (79.3%)
  - 36-54: 8 (13.8%)
  - < 35: 3 (5.2%)
  - Unknown: 1 (1.7%)
- Heart Transplantation: 1 patient (1.7%)
- Repeat Cardiac Hospitalizations: 34 patients (58.6%)
  - Number repeat hospitalizations: median 2 (range 0-21)
- Death: 3 (5.2%)
- Stroke: 3 (5.2%)
- Recurrent Myocardial Infarction: 12 (20.7%)
- ICD Implantation: 4 (6.9%)
Repeat Revascularization

- Total Patients: 15 (25.9%)
- Stent Related Complications: 10 (15.5%)
  - Stent Thrombosis: 2 (3.4%)
  - Restenosis: 5 (8.6%)
  - Residual Stenosis: 2 (3.4%)
  - Stent Mal-apposition: 1 (1.7%)
- SCAD Recurrence requiring PCI with stenting: 5 (8.6%)
- Multiple Interventions: 2 patients (3.4%)

(Saw Circ Cardiovasc Interv. 2014;7:645-655.)

Iatrogenic Dissection

- 3.4% of SCAD Patients vs <0.2% general population
- Increased Risk
  - Radial approach
  - Deep catheter intubation

Non-coronary dissections


False Lumen Stenting


Dissection Propagation

SCAD in High OM  Stent Inflation  Dissection Propagation


Late Hematoma Resorption with Stent Malapposition

9 days after PCI for mLAD SCAD

PCI Techniques

- Implanting long drug-eluting stents with 5-10mm overlap on proximal and distal edges
- Direct stenting
- Balloon Angioplasty without PCI
- Cutting balloons to decompress hematoma
- Sealing distal and proximal ends prior to middle of the hematoma


PCI Is NOT Protective From Recurrent SCAD

Recursive SCAD
Revascularization vs Conservative Management

Coronary Artery Bypass Grafting

- Considered Left Main or Proximal Dissections
- High Early Rates of Revascularization
  - 20 patients, 32 of 34 intended targets re-vascularized
- High Rates of Late Graft Failure
  - 11/16 graft failures in 11 of 20 patients imaged during follow-up
- Not protective from recurrent SCAD


Summary Acute Management

Management of acute spontaneous coronary artery dissection (SCAD)

- Clinically stable, no high-risk anatomy
- Clinically stable with left main or severe proximal 2-vessel dissection
- Active/ongoing ischemia or hemodynamic instability

- Conservative therapy
  - Monitor as inpatient 3-5 days
- Consider CABG
  - Conservative Rx may be reasonable (not studied)
- Consider PCI if feasible
  - OR
  - Urgent CABG (based on technical considerations and local expertise)
Medical Therapy

- No randomized trials

Anticoagulation and Antiplatelet Therapy

- Heparin - Discontinue
  - Theoretical risk worsening dissection
- Aspirin - Continue
  - Minimum 1 year, possibly indefinitely
- Dual Antiplatelet Therapy
  - Published series predominantly use clopidogrel
  - Follow standard recommendations for PCI
  - Unclear benefit or duration in use for conservative management
  - Consider 1-3 months in conservatively treated patients
Life Long Beta- Blocker Therapy

Treat Hypertension

- Ace-I / ARB
- LV systolic dysfunction
- Fibromuscular dysplasia
- Calcium Channel Blockers
- Anti-anginal

[Saw J Am Coll Cardiol 2017;70:1148–58]
Statin Therapy

- Tweet et al in a series of 87 patients found higher recurrence rate with statin use
- Saw et al in series of 327 patients found no association with SCAD recurrence and statin use
- Recommended for primary prevention

Antianginal Therapy

- Chest pain after SCAD is common ~50%
  - Exertional and Non-exertional
  - Mental Stress
    - Anxiety and depression in ~40% of patients following SCAD
  - Menstrual cycle
- Treatment
  - Short and long acting nitrates
  - Calcium channel Blockers
  - Ranolazine
  - Treat associated anxiety and depression
Medial Therapy- Summary

- Discontinue heparin
- Aspirin and beta blocker therapy life long
- Dual antiplatelet individualize recommendation
- ACE-I or ARBs for hypertension or LV systolic dysfunction
- Statins if meet criteria for primary prevention
- Antianginal therapy for post-SCAD chest pain

All SCAD Patients Should Be Referred for Cardiac Rehabilitation

- Starting goals exercise
  - BP max 130/80
  - HR 50-70% of heart rate reserve
  - Free weights: 2-12lbs to start
    - Working up to 20lbs women
    - Working up to 50lbs men
    - Low resistance and high repetition

- Avoid
  - Strain / Valsalva maneuvers
  - High intensity activities
  - High contact sports
  - Pushing to exhaustion
  - Extreme temperatures
  - Abrupt increases in physical activity (Hot Yoga)
Long-term Complications at median follow-up of 3.1 years

- Death: 1.2%
- Recurrent infarction: 16.8%
- Stroke / TIA 1.2%
- Recurrent SCAD: 10%
- Unplanned revascularization: 5.8%

(SAW J Am Coll Cardiol 2017;70:1148–58)

Heart Failure

- All SCAD Patients should have LV EF assessment prior to discharge
- LV EF <50%: 21.8% at presentation in a series of 327 patients
- Heart Failure Requiring Advanced Therapies at MHI
  - 2 Heart Transplants
  - 1 Left Ventricular Assist Device
Overall Survival Excellent


Recurrence is Common

Pregnancy Associated SCAD

1. 1.81 SCAD events per 100,000 pregnancies
2. Most common etiology of MI among pregnant and post-partum women
3. 4% of MHI SCAD Patients
4. Higher complication rate
5. Acute management same as non-pregnancy SCAD
6. Less likely to be associated with Fibromuscular Dysplasia

Most Pregnancy Associated SCAD in Post-Partum

Pregnancy and Hormone Counseling with SCAD

- Pregnancy Counseling
  - Recommend against pregnancy, but data limited support recommendation
  - Preconception counseling if someone desires pregnancy (MHI Cardio-Pregnancy Program)
- Hormone Therapy
  - Non-hormonal contraceptives (IUD with progestin preferred)
  - Avoid Hormone Replacement Therapy
- Medications Contraindicated in pregnancy
  - Statins
  - Atenolol
  - Ace-inhibitors


Fibromuscular Dysplasia

- Non-inflammatory non-atherosclerotic disorder that leads to arterial stenosis of small to medium sized vessels
- Aneurysm, tortuosity, and dissections of small to medium sized vessels common

Renal Artery  Carotid Arteries  Femoral Artery  Coronary Artery

Fibromuscular Dysplasia Management

- Aspirin 81mg daily for life for thrombosis prevention
- Blood pressure management
  - Ace-I / ARBs for renovascular involvement
  - Beta Blockers for SCAD
  - Beta Blockers, Calcium channel blockers, ARBs for Migraines
- Migraines
  - Avoid Triptans / Vasoconstrictive medications
- Smoking Cessation


Conclusions

- Diagnosis can be challenging
- Multimodality Imaging
- Acute Management
  - Keep inpatient for minimum 2-3 days
  - Aspirin / Beta Blockers / Clopidogrel
  - Look for Fibromuscular Dysplasia
- Long Term Management
  - Continue Beta Blockers
  - Manage Blood Pressure
  - Pregnancy / Hormone Therapy Counseling