Statins, Beta Blockers and Anti-Platelet Agents

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Professor of Clinical Anesthesia
University of California, San Francisco

Lecture Objectives
• Pertinent epidemiology, physiology, pharmacology associated with aging
• Evidence for perioperative efficacy and safety in the elderly of:
  – Statins
  – Beta Blockers
  – Antiplatelet agents

Disclosures
• No financial disclosures

Epidemiology, Physiology & Pharmacology
Improving Periop Outcomes

- Cardiovascular
- Renovascular
- Cerebrovascular
  - Stroke/TIA
  - Delirium
- Peripheral Vascular
  - Arterial
  - Venous
    - Pulmonary Embolism
- Major Non-Vascular
  - Sepsis

ACC/AHA Periop Evaluation Guidelines

Size of Treatment Effect

- Class I: Benefit >>> Risk
  - SHOULD USE
- Class IIa: Benefit >>> Risk, more studies needed
  - IS REASONABLE TO USE
- Class IIb: Benefit >= Risk, more studies needed
  - MAY BE CONSIDERED
- Class III: Risk > Benefit
  - DON’T USE
Secondary Prevention AHA

- **Beta Blockers**
  - I(A): PostMI, ACS, LVSD (indefinitely)
  - IIa(C): CAD, Vascular Disease, AODM
- **Statins**
  - I(A): LDL-C < 100 mg/dl
- **Antiplatelets**
  - I(A): ASA 75 - 162 mg indefinite
  - I(B): Clopidogrel 75 mg up to 1 yr after ACS or PCI

AHA/ACC Guideline

AHA/ACC Guidelines for Secondary Prevention for Patients With Coronary and Other Atherosclerotic Vascular Disease: 2006 Update

Endorsed by the National Heart, Lung, and Blood Institute

Sidney C. Smith, Jr, MD; Jentlyn Allen, RN, ScD; Steven N. Blair, PhD; Robert O. Bonow, MD; Lawrence M. Brass, MD; Gregg C. Fonarow, MD; Scott M. Grundy, MD, PhD; Loren Hatanaka, MD; Daniel Jones, MD; Riafan M. Krumholz, MD, FACP; Luri Mosca, MD, PhD; MPP; Richard C. Pasternak, MD; Thomas Pearson, MD, MPH, PhD; Marc A. Pfeffer, MD, PhD; Kathryn A. Tieberg, PhD

Circulation 2006
Lipid-Lowering Therapy With Statins in High-Risk Elderly Patients: The Treatment-Risk Paradox

Deedwania EHJ 2004

N = 396,077 patients > 65 yrs with Hx CAD or DM
Only 19% were prescribed statins

Efficacy in Systolic Heart Failure (MERIT-HF)

Table 1. Baseline characteristics in patients in the two age groups

Drug Tolerance and Withdrawal

Deedwania EHJ 2004

Likelihood of receiving therapy decreases by 6.4% per year age
Aging: Major CV Effects

- CV stiffening
- Conduction system disease
- Impaired Beta-adrenergic responsiveness
- Impaired endothelial function
- Decreased baroreceptor responsiveness
- Impaired preconditioning/oxidative capacity

Epidemiology of Risk Factors in Aging
CRUSADE ACS Registry (>55,000 pts)

Pharmacokinetics/Dynamics with Aging

CRUSADE/VIGOUR COHORTS
**Statins**

**Statin Effects**
- Lipid Dependent
  - Reduce LDL cholesterol (HMG-CoA)
- Lipid Independent (pleiotropic)
  - Inhibit isoprenoids that bind to Rho GTPs
  - Anti-inflammatory
  - Vasodilatory
  - Anti-thrombotic/plaque stabilization

**Secondary Prevention AHA**
- Statins
  - I(A): LDL-C < 100 mg/dl
5 Year NNT values to prevent 1 major CV complication

Ridker Circ Outcomes 2009

Elderly less likely Elderly more likely

Adjusted OR (95% CI)

Fig 2. Association of the prescription of medical therapy with elderly age.

Statin use in the elderly: Results from a peripheral vascular survey in The Netherlands

Sanne E. Hoeks, MSc,a Wilma J. Scholte op Reimer, PhD,a Olaf Schommer, MD,a Marrie J. Lenssen, PhD,a Henk van der Meulen, MD, PhD,a and Evert van Dijk, MD, PhD,a Rotterdam, The Netherlands

N = 711 pts 42% > 70 yrs.

Fig 3. Proportion of patients with statin therapy by age groups.

J Vasc Surg 2008
Fluvastatin and Perioperative Events in Patients Undergoing Vascular Surgery

Olaf Schouten, M.D., Ph.D., Eric Boersma, Ph.D., Sanne E. Hoeks, M.Sc., Robbert Benner, Ph.D., Hero van Urk, M.D., Ph.D., Marc R.H.M. van Sarnbeeck, M.D., Ph.D., Hennie J.M. Verhagen, M.D., Ph.D., Nisar A. Khan, Ph.D., Martin Dunkergrun, M.D., Ph.D., Jeroen J. Bax, M.D., Ph.D., and Don Poldermans, M.D., Ph.D., for the Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echocardiography Study Group

Fluvastatin 80 mg 37 days preop to 30 days postop

NEJM/2009

Table 1. Baseline Characteristics of the Patients, According to Study Group. a

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Fluvastatin (N = 250)</th>
<th>Placebo (N = 247)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographic Characteristics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age — y</td>
<td>66.0 ± 10.5</td>
<td>65.8 ± 11.5</td>
</tr>
<tr>
<td>Male sex — no. (%)</td>
<td>194 (77.6)</td>
<td>178 (72.1)</td>
</tr>
<tr>
<td><strong>Risk factors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myocardial infarction — no. (%)</td>
<td>73 (29.2)</td>
<td>66 (26.7)</td>
</tr>
<tr>
<td>Angina pectoris — no. (%)</td>
<td>52 (20.8)</td>
<td>59 (23.9)</td>
</tr>
<tr>
<td>Congestive heart failure — no. (%)</td>
<td>13 (5.2)</td>
<td>19 (7.7)</td>
</tr>
<tr>
<td>Diabetes mellitus — no. (%)</td>
<td>55 (22.0)</td>
<td>42 (17.0)</td>
</tr>
</tbody>
</table>
Holter Ischemia (p = 0.01) NNT 12

CV death or NonFatal MI (p = 0.03) NNT 19

Placebo

Fluvastatin

Fluvastatin
1006 intermediate cardiac risk patients
Nonvascular NCS
Fluvastatin 80 mg/Bisoprolol 2.5 mg
Preop 34 days/postop 30 days

Myocardial Infarction

<table>
<thead>
<tr>
<th>Event</th>
<th>Odds Ratio (95% CI)</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCI</td>
<td>0.51 (0.27, 0.97)</td>
<td>10.69</td>
</tr>
<tr>
<td>Verduzco et al</td>
<td>0.61 (0.31, 1.19)</td>
<td>6.67</td>
</tr>
<tr>
<td>MAPLES II</td>
<td>0.60 (0.40, 0.91)</td>
<td>26.48</td>
</tr>
<tr>
<td>Jia et al</td>
<td>0.58 (0.36, 0.93)</td>
<td>0.92</td>
</tr>
<tr>
<td>ARYTA-RECAPTURE</td>
<td>0.39 (0.17, 0.85)</td>
<td>5.69</td>
</tr>
<tr>
<td>ARYTA-ACS</td>
<td>0.56 (0.35, 0.90)</td>
<td>5.89</td>
</tr>
<tr>
<td>Kito et al</td>
<td>0.55 (0.22, 1.34)</td>
<td>1.66</td>
</tr>
<tr>
<td>Bowles et al</td>
<td>0.33 (0.12, 0.99)</td>
<td>0.95</td>
</tr>
<tr>
<td>ARYTA</td>
<td>0.29 (0.16, 0.59)</td>
<td>3.89</td>
</tr>
<tr>
<td>Bilgen et al</td>
<td>0.63 (0.34, 1.16)</td>
<td>21.49</td>
</tr>
<tr>
<td>Subtotal (unadjusted)</td>
<td>0.55 (0.47, 0.64)</td>
<td>93.27</td>
</tr>
</tbody>
</table>

CAASG
Ji et al | 0.32 (0.09, 1.42) | 0.41   |
Mintz et al | 0.16 (0.06, 0.41) | 0.74   |
Sing et al | 2.06 (0.10, 41.48) | 0.74   |
ARYTA-J | 0.98 (0.34, 2.80) | 1.66   |
Chow et al | 0.08 (0.00, 1.47) | 0.51   |
Subtotal (unadjusted) | 0.65 (0.34, 1.39) | 4.89   |

NON CORONARY SURGERY
DECREASE-B | 0.46 (0.29, 0.76) | 6.26   |
DECREASE-A | 0.51 (0.2, 1.31) | 6.84   |
Doros et al | 0.38 (0.11, 1.23) | 2.86   |
Subtotal (unadjusted) | 0.47 (0.26, 0.88) | 15.64  |

Overall (unadjusted) | 0.57 (0.45, 0.70) | 100.00 |

NOTE: Weights are from random effects analysis.

Favors Statin  Favors Control
Although overall risk was not reduced, once it occurred mortality for patients with MODS, adverse effects of surgical complications, and any complication (?) was.
Consequences of Succinylcholine Administration to Patients Using Statins

Aparnasri Turan, M.D.† Maria L. Mendez, M.D.,† Shilpa Gupta, M.S.,‡ Jing You, M.S.,§ Alexandru Gottlieb, M.D.,† Wei Han Chu, M.D.,‡ Leif Seager, M.D.,# Daniel L. Sassler, M.D.,**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Statin (N = 38)</th>
<th>Nonstatin (N = 32)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>61 ± 9</td>
<td>57 ± 10</td>
</tr>
<tr>
<td>Sex (female), no. (%)</td>
<td>16 (42)</td>
<td>15 (47)</td>
</tr>
<tr>
<td>Race (white), no. (%)</td>
<td>37 (97)</td>
<td>29 (91)</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>91 ± 24</td>
<td>93 ± 24</td>
</tr>
<tr>
<td>Height, cm</td>
<td>172 ± 10</td>
<td>172 ± 12</td>
</tr>
</tbody>
</table>

More intense fasiculations but no difference in K+, CK or muscle pain

Statins and Incident Diabetes

<table>
<thead>
<tr>
<th>Study</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>WOSCOPS Pravastatin (Hypothesis Generating Trial)</td>
<td>0.70 (0.50–0.98)</td>
</tr>
<tr>
<td>HPS Simvastatin</td>
<td>1.20 (0.98–1.35)</td>
</tr>
<tr>
<td>ASCOT-LLA Atorvastatin</td>
<td>1.20 (0.91–1.44)</td>
</tr>
<tr>
<td>PROVE-IT Atorvastatin VS Pravastatin</td>
<td>1.11 (0.67–1.83)</td>
</tr>
<tr>
<td>CORONA Rosuvastatin</td>
<td>1.13 (0.86–1.50)</td>
</tr>
<tr>
<td>JUPITER Rosuvastatin</td>
<td>1.25 (1.05–1.54)</td>
</tr>
</tbody>
</table>

Myoglobin (µg/L)

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Statin user</th>
<th>Non-statin user</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>5</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>20</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>24</td>
<td>150</td>
<td>150</td>
</tr>
</tbody>
</table>

More intense fasiculations but no difference in K+, CK or muscle pain
Statin Withdrawal Studies

- Schouten et al. Am J Cardiol 2007
  - 298 vascular pts., 2000 - 06
  - Interruption in 23%, median 3 days
  - H.R. troponin release 4.5 (22. - 9.6)
  - 669 vascular pts., 2001 - 03
  - 491 pts prior to guideline for restarting
  - 178 pts post guideline
  - Median delay 4 vs 1 day postop
  - R.R. myonecrosis 5.4 (1.2 - 25.3)

Beta Blockers

ACC/AHA Guidelines

- Stable Angina
  - Class IA, IB
- ST elevation MI
  - Class IA
- Unstable Angina/Non ST elevation MI
  - Class IB
- CHF
  - Class IA, IB
Secondary Prevention AHA

- Beta Blockers
  - I(A): PostMI, ACS, LVSD (indefinitely)
  - IIa(C): CAD, Vascular Disease, AODM

Beta Blocker Pharmacology

<table>
<thead>
<tr>
<th></th>
<th>Select</th>
<th>Form</th>
<th>Dose</th>
<th>Elim</th>
<th>CHF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atenolol</td>
<td>B1</td>
<td>PO, IV</td>
<td>QD</td>
<td>R</td>
<td>-</td>
</tr>
<tr>
<td>Bisoprolol</td>
<td>B1</td>
<td>PO</td>
<td>QD</td>
<td>R, H</td>
<td>+/-</td>
</tr>
<tr>
<td>Carvedilol</td>
<td>Non, A</td>
<td>PO</td>
<td>BID</td>
<td>H</td>
<td>+</td>
</tr>
<tr>
<td>Labetolol</td>
<td>Non, A</td>
<td>PO, IV</td>
<td>IV</td>
<td>H</td>
<td>-</td>
</tr>
<tr>
<td>Metoprolol Tartrate</td>
<td>B1</td>
<td>PO, IV</td>
<td>BID+</td>
<td>H</td>
<td>+</td>
</tr>
<tr>
<td>Metoprolol Succin</td>
<td>B1</td>
<td>PO</td>
<td>QD</td>
<td>H</td>
<td>+</td>
</tr>
<tr>
<td>Propranolol</td>
<td>Non</td>
<td>PO, IV</td>
<td>TID+</td>
<td>H</td>
<td>-</td>
</tr>
</tbody>
</table>

Mechanisms of BB protection

- Reduction in heart rate (diastolic time)(++)
- Reduction in contractility (++)
- Preservation of contractile function (++)
- Anti-arrhythmic effects (+)
- Plaque “stabilization” (?)
- Reduction of athero burden (?)
- Anti-inflammatory/oxidant effects (?)
- Blunting of hyper-coagulability (?)
- Restoration of Heart Rate Variability (?)
- Enhancement of endothelial function (-)
Age associated decline in max HR and LV contractility responses are a manifestation of decreased Beta adrenergic sensitivity

Circulation 1994

Effect of Aging on Atenolol Pharmacokinetics and Pharmacodynamics

Atenolol 100 mg po qd x 7
Bicycle Exercise testing with venous sampling

J Clin Pharm 1995
National VA Data: Beta Blocker Exposure DOS or POD1 (N = 76,000)

BB’s: What’s not to like?
AHA Scientific Statement

Treatment of Hypertension in the Prevention and Management of Ischemic Heart Disease
A Scientific Statement From the American Heart Association Council for High Blood Pressure Research and the Councils on Clinical Cardiology and Epidemiology and Prevention

Clive Rosenfield, MD, PhD, FAHA; Chair; Henry R. Black, MD; Christopher P. Cannon, MD, FAHA; Bernard J. Gersh, MB ChB, DPhil, FAHA; Joel Gress, MD, FAHA; Joseph L. Levy, Jr, MD; Norman M. Kaplan, MD; Christopher M. O’Connor, MD, FAHA; Patrick T. O’Gara, MD, FAHA; Suzanne Oparil, MD, FAHA

However, in patients who do not have symptomatic CAD, have not had an MI, or do not have HF, the evidence for B-blocker cardioprotection is weak, especially in the elderly, and there are other studies that suggest a relative lack of benefit on cerebrovascular and renal disease end points.

Circulation 2007;115:2781-88

Effects of extended-release metoprolol succinate in patients undergoing non-cardiac surgery (POISE trial): a randomised controlled trial

POISE Study Group

<table>
<thead>
<tr>
<th></th>
<th>Metoprolol group (N=417)</th>
<th>Placebo group (N=417)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>68.9 (10.5)</td>
<td>69.1 (10.4)</td>
</tr>
<tr>
<td>Sex (female)</td>
<td>1549 (72.1%)</td>
<td>1509 (72.1%)</td>
</tr>
<tr>
<td>Perioperative heart rate (beats per minute)</td>
<td>776 (12.2)</td>
<td>783 (12.4)</td>
</tr>
<tr>
<td>Perioperative blood pressure (mm Hg)</td>
<td>138.7 (19.7/78.3 (11.3)</td>
<td>138.7 (19.7/79.5 (11.3)</td>
</tr>
</tbody>
</table>

Lancet 2008
Primary Outcome MI

CV death, MI, cardiac arrest

Cardiovascular Response to Acute Anemia
Weiskopf et al JAMA 1998
Proposed Mechanisms of stroke

- Beta blockers inhibit compensatory increase in CBF during anemia
  - Limiting HR
  - Inhibiting cerebral vasodilatation
    - Cerebral vessels seem more sensitive
And PLEASE don’t forget the Beauty and Wonder of “Cardiac Output”!!

BB Withdrawal Studies

- 1975 Miller (NEJM)
  - 20 ambulatory pts studied over 44 week period
- 1981 Goldman
  - 2 cases only
- 1982 Ponten
  - RCT of withdrawal in NCS, higher MI rate in Rx!
- 1985 Walker
  - Angina patients, increase HR but no adverse effects
- 1986 Croft
  - Withdrawal in Acute MI, no adverse effects (but increased chest pain first 24 hrs.)
BB Withdrawal Studies

- 1996 Mangano
  - 8 patients withdrawn for placebo, ? No problems
- 2001 Shammash
  - 2 centers, mid-1990’s, 8 patients records reviewed
    • Mortality Odds ratio 65 (!)
- 2007 Hoeks
  - Longterm outcome study of vascular surgery
    • 3% of 711 total patients (53% had no use): 24% 30 day mortality, 38% 1 year mortality
- 2009 Van Klei
  - 25% of 18% of patients taking BB on admit were discontinued (at some point in hospital)
  - Odds ratio for POMI 2.0 (1.1 - 3.9) p < 0.04

SFVAMC BB Analysis 1996 - 2008

<table>
<thead>
<tr>
<th></th>
<th>30 d Mortality</th>
<th>1 yr Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Use</td>
<td>reference</td>
<td>reference</td>
</tr>
<tr>
<td>Addition</td>
<td>0.5 (0.3 - 0.8)</td>
<td>0.6 (0.5 - 0.8)</td>
</tr>
<tr>
<td>Continuous</td>
<td>0.7 (0.5 - 0.98)</td>
<td>0.8 (0.7 - 1.0)</td>
</tr>
<tr>
<td>Withdrawal</td>
<td>3.9 (2.6 - 6.0)</td>
<td>2.0 (1.5 - 2.6)</td>
</tr>
</tbody>
</table>
A regional quality improvement effort to increase beta blocker administration before vascular surgery

Philip P. Goodney, MD, MS,* Jeni Eldrup-Jorgensen, MD,* Brian W. Nolan, MD, MS,*
Daniel J. Burgers, MD,* Donald S. Lilienky, PhD,** and Jack L. Cramerco, MD,** for the Vascular Study Group of New England, Lebanon and Hanover, NH; Portland, ME; and Burlington, VT

N = 3,049 Vascular Patients
6 hospitals, 29 surgeons
2003 - 2008

J Vasc Surg 2011
Class I 2009 Update

1. Use for Class I ACC/AHA Indications (level C)
   - Use in recent past for angina, arrhythmia, HTN (level C) **Change in terminology**
   - DECREASE patients (Vascular Ischemia Preop Testing) (B)
     - **Change in terminology** (CAD or ischemia)
     - **Reduced to IIa recommendation**

Class III 2009 Update

1. Absolute Contraindication to BB’s (level C)
2. **POISE Clause**
   - "Routine Administration of beta blockers in the absence of dose titration is not useful and may be harmful to patients not currently taking beta blockers…"

BB Institution and Titration

- Initiation of Rx well before planned procedure with careful titration to achieve adequate heart rate control (60 to 80 bpm) while avoiding frank bradycardia or hypotension is suggested.
- In the management of perioperative patients fixed-dose administration has not shown sufficient benefit to warrant routine use.
- Long acting beta blockade might be superior to short-acting, but clinical trial evaluation is awaited to confirm this.
Chronic β Blockade Is Associated with a Better Outcome after Elective Noncardiac Surgery than Acute β Blockade

A Single-center Propensity-matched Cohort Study

Christoph Ellenberger, M.D.,* Gordon Tai, Ph.D.,† W. Scott Beattie, M.D., Ph.D., F.R.C.P.C.,‡

N = 10,691 pts.
-3 Toronto teaching hospitals
-Elective NCS
-2008 - 2010
-Prospective electronic databases

Anesthesiology 2011
Canadian Controversy!!!!!!

Eh?  Eh Eh?

Statin Good!  Beta Blocker Bad!

<table>
<thead>
<tr>
<th>Variable</th>
<th>Coefficient estimate</th>
<th>Odds ratio estimate</th>
<th>95% Wald confidence interval</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of CVA/TIA</td>
<td>0.9728</td>
<td>3.64</td>
<td>1.57-4.45</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Preoperative depression</td>
<td>1.27</td>
<td>3.56</td>
<td>1.53-8.28</td>
<td>0.003</td>
</tr>
<tr>
<td>Age</td>
<td>0.044</td>
<td>1.04</td>
<td>1.02-1.07</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
| Preoperative beta blocker
administration | 0.722                | 2.06                | 1.18-3.46                   | 0.011   |
| Preoperative statin
administration | 0.245                | 1.32                | 1.37-0.88                   | 0.011   |

Delirium following vascular surgery: increased incidence with preoperative β-blocker administration

Le delirium après une chirurgie vasculaire: incidence accrue lors de l’administration préopératoire de β-bloquants

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Taking statins</th>
<th>Not taking statins</th>
</tr>
</thead>
<tbody>
<tr>
<td>n = 19 501</td>
<td>n = 264 657</td>
<td></td>
</tr>
<tr>
<td>Age (yr, mean (SD))</td>
<td>71.9 (4.7)</td>
<td>73.9 (6.1)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>10 097 (51.9)</td>
<td>132 621 (50.1)</td>
</tr>
<tr>
<td>Male</td>
<td>9 404 (48.2)</td>
<td>132 036 (49.9)</td>
</tr>
</tbody>
</table>
Statin Bad!

Statin Good!

Preoperative Use of Statins Is Associated with Reduced Early Delirium Rates after Cardiac Surgery

I told you that statins alter cerebral autoregulation via effects on eNOS!

Beta blockers screw up cerebral blood flow and melatonin release!
Anti-Platelet Agents

Aspirin Efficacy in CV Diseases

Secondary Prevention AHA

- Antiplatelet Agents
  - I(A): ASA 75 - 162 mg indefinite
  - I(B): Clopidogrel 75 mg up to 1 yr after ACS or PCI
Aspirin Withdrawal Studies

- Oscarsson et al. BJA 2010 RCT
  - 220 non-vascular NCS pts
  - ASA 7 days preop to 3 days postop
  - RRR 80% in MACE at 30 days
- Mantz et al. BJA 2011 (STRATAGEM) RCT
  - 291 non-vascular NCS pts
  - ASA 10 days preop to 30 days postop
  - No diff in thrombotic/bleeding complices

Class III
1. It is not recommended that routine prophylactic coronary revascularization be performed in patients with stable CAD before noncardiac surgery. (Level of Evidence: B)
2. Elective noncardiac surgery is not recommended within 4 to 6 weeks of bare-metal coronary stent implantation or within 12 months of drug-eluting coronary stent implantation in patients in whom thienopyridine therapy, or aspirin and thienopyridine therapy, will need to be discontinued perioperatively. (Level of Evidence: B)
Black Box Warnings

**Diclofenac sodium enteric-coated tablets**

- Tablets of 25 mg, 50 mg, and 75 mg
- Rx only
- Prescribing information

**Cardiovascular Risk**

- NSAIDs may cause an increased risk of serious cardiovascular thrombotic events, myocardial infarction, and stroke, which can be fatal. This risk may increase with duration of use. Patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk. (See WARNINGS.)
- Voltaren® (diclofenac sodium enteric-coated tablets) is contraindicated for the treatment of perioperative pain in the setting of coronary artery bypass graft (CABG) surgery (see WARNINGS).

Aspirin/NSAIDs Interactions

- Competitive inhibition of cyclooxgenase at the platelet receptor binding site reduces aspirin antiplatelet effects.
- NSAIDs should be dosed at least 30 min to 2 hrs after ASA or 8 - 10 hours prior.

Stepped Care Approach to Pharmacologic Therapy for Musculoskeletal Symptoms With Known Cardiovascular Disease or Risk Factors for Ischemic Heart Disease

- Acetaminophen, ASA, tramadol, narcotic analgesics (short term)
- Nonacetylated salicylates
- Non COX-2 selective NSAIDs
  - NSAIDs with some COX-2 activity
  - COX-2 Selective NSAIDs

What’s on the Horizon?
Ongoing or Planned Trials

- **POISE-2**
  - RCT of clonidine/ASA 2 - 4 hrs preop for 30 days in 10,000 pts undergoing NCS.
- **DECREASE XIII**
  - RCT: Esmolol with optimal Rx for HR control for 72 hrs in 260 Vascular patients.
- **DECREASE VII**
  - RCT: clopidrogel and ASA in 750 Vascular patients with postop troponin elevation
- **OBTAIN Registry**
  - E.S.A. Registry of 1400 PCI pts within 4 yrs
  - Propensity Matching evaluate 1 or 2 agent antiplatelet Rx

Conclusions

- Getting old is tough! (literally!)
- “Take your medicine” (before and after surgery) (BBs, statins and ASA) generally is good advice, particularly for the elderly and in most, but not all, situations supported by the literature.
Conclusions

• Getting old is tough! (literally!)
• “Take your medicine” (before and after surgery) (BBs, statins and ASA) generally is good advice, particularly for the elderly and in most, but not all, situations supported by the literature.
• Starting new medication in naive patients (or substituting medications into an existing regimen) is always more complex than it seems.

Conclusions

• Following existing AHA Guidelines is probably the best way to practice.
• Be patient! Keep your ear to the ground since there is lots more information (and probable controversy) coming!