Management of Chronic Coronary Syndromes Robert J. Chilton, DO, FACOI

No Disclosures

CHRONIC STABLE ANGINA BY THE GUIDELINES

Global Risk Reduction--WINS

Picking Mom and Dad-2016



Environmental

Vascular / Tissue

Metabolics

Stop smoking-1B Physical activity-1B Weight control-1B Chelation therapy-3C Influenza vaccination-1B

Blood pressure-1B RAAS blockade-1A Aldosterone blockade-1A/B

Lipids-1B Triglycerides-1B Diabetes-1B Antiplatelets-1A/B

Circulation. 2007;116:2762-2772

50 y/o he presents with increasing fatigue and short of breath on exercise

BP 145/90 LDL cholesterol 140 mg/dl HDL cholesterol 35 Triglycerides 280



Patient from San Antonio





Yearly mortality (death) in medically treated patients by coronary angiogram



Adapted from al Patel et al

50 year old male

Years of life remaining



Eur Heart J 2002; 23: 458–466

Framingham 40 year follow up N=5070



60 year old male



Framingham 40 year follow up N=5070



Johns Hopkins: medical students cholesterol and risk of CV disease

- Prospective study
- N=1017 young men
- Mean age 22
- 27-42 years follow up
 - Median 30.5 years
- Endpoint: risk of CV disease and total mortality associated with cholesterol

Variable	All Subjects	Qu	P VALUET			
		118–172 mg/dj	173-189 mg/dl	190–208 mg/di	209-315 mg/dl	
No. of subjects	1017	250	258	254	255	
Age (yr)	22.0±2.3	21.6±1.9	21.8±2.0	21.8±2.0	22.7±3.1	0.001
Coffee intake (cups/day)‡	2.3±1.8	3.1±1.9	2.2±1.8	2.3±1.7	2.4±1.9	0.2
Body-mass index	23.2±2.6	22.5±2.4	22.8±2.2	23.4±2.6	24.0±2.9	0.001
Systolic blood pressure (mm Hg)	1 25±14	124±14	126±15	125±14	126±14	0.3
Diastolic blood pressure (mm Hg)	75±9	74±9	75±10	75±9	76±10	0.2
Serum cholesterol (mg/dl)	192±29	158±11	181±5	199±6	231±20	_

NEJM 1993;328:313



Note: it starts mainly after 15-20yrs



NEJM 1993;328:313 🦬

"The guidelines"



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na Focused Update

na Focused Update of the lelines for the Management **Chronic Stable Angina**

of Cardiology/American Heart Association s Writing Group to Develop the Focused the Management of Patients With Chronic

007;116:2762-2772

t include Westyle and phermatcherapy / JR 3	Added recommendation			
2002 Chronic Angina Recommendations		N7 Chrunic Angina Recommendations	2007 COR and LOE	Converts
	Renin Angiotensia	-Aldostenuse System Blockers (Continued)		
	Angiotensin rec have hyperta antibitors, hu with lieft ven	optor blockers are recommended for gotients who makes, have indications for but are insteamt of ACE we heart Johns, or have had a myscardial influction blocker ejection itsection less then or equal to 40%.	100	New recommendation
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be harmful because of its potential to cause hypocalcemia.

Pharmacotherapy for Chronic Stable Angina (class I)

- 1. Aspirin in the absence of contraindications A
- 2. Beta-blockers as initial therapy in the absence of contraindications in patients with prior myocardial infarction or without prior myocardial infarction A,B
- 3. ACE inhibitor in all patients with CAD who also have diabetes and/or LV systolic dysfunction A
- 4. LDL-lowering therapy in patients with documented or suspected CAD and LDL cholesterol >130 mg/dl, with a target LDL of <100 mg/dl A
- Sublingual nitroglycerin or nitroglycerin spray for the immediate relief of angina B
- 6. Calcium antagonists <u>t</u> or long-acting nitrates as initial therapy for reduction of symptoms when beta blockers are contraindicated B



Pharmacotherapy for Chronic Stable Angina (class IIa)

- 1. Clopidogrel when aspirin is absolutely contraindicated
- 2. Long-acting non-dihydropyridine calcium antagonists <u>t</u> instead of beta blockers as initial therapy B
- In patients with documented or suspected CAD and LDL cholesterol 100–129 mg/dl, several therapeutic options are available: B
 - a. Lifestyle and/or drug therapies to lower LDL to <100 mg/dl
 - b. Weight reduction and increased physical activity in persons with the metabolic syndrome
 - c. Institution of treatment of other lipid or non-lipid risk factors; consider use of nicotinic acid or fibric acid for elevated triglycerides or low HDL cholesterol
- 4. ACE inhibitor in patients with CAD or other vascular disease



Pharmacotherapy for Chronic Stable Angina

- IIb (weak supportive evidence)
 - Low-intensity anticoagulation with warfarin in addition to aspirin B
- III (not indicated)
 - 1. Dipyridamole B
 - 2. Chelation therapy B



Ranolazine- new first line indication for the treatment of chronic angina



Lipids are still #1 and smoking #2

9 Modifiable Factors Account for 90% of First MI **Abnormal lipids** Lipids 50 Smoking Smoking 50 Hypertension Abd Obesity 36 Diabetes 40 Abdominal obesity Diabetes 30 20 18 20 Psychosocial 10 **INTERHEART** Trial 10 Physical activity 0 Fruits/vegetables % PAR Yusuf S et al. Lancet. 2004:364:937-52

PAR = population attributable risk, adjusted for all risk factors

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Alcohol

Tight blocks have usually more healed plaque ruptures



Environmental	Stop smoking-1B Physical activity-1B Weight control-1B Chelation therapy-3C Influenza vaccination-1B
/ascular / Tissue	Blood pressure-1B RAAS blockade-1A Aldosterone blockade-1A/B
Metabolics	Lipids-1B Triglycerides-1B Diabetes-1B Antiplatelets-1A/B



Importance of genetic factors when picking your parents



Selected risk factor variables in offspring ages 18 to 31 years by parental history of disease, race, and sex

Vascular / Tissue

- Blood pressure-1B
 - Lifestyle (low salt, weight control and exercise
 - Moderate etoh & vegetables
 - BP <140 / 90 by JNC VII-HCTZ
 - Diabetes & CRDx 130 / 80
 - HT with CAD—BB &/or ACEI
- RAAS blockade-1A
 - EF<40 ACEI
 - Mild/moderate risk & normal EF-2B
- Aldosterone blockade-1A/B
 - After MI (normal kid function & K+)
 - Patients already on BB & ACEI
 - EF<40 with HF or diabetes

N Engl J Med. 2003;348:1309-1321 EPHESUS N Engl J Med. 1999;341:709-717 RALES



Myocardial Oxygen Consumption Factors MVO₂

- Heart Rate
 - Most important
- Myocardial wall tension
 - Pressure
 - Volume
 - Thickness
- Contractility

σ=Wall Tension P=Pressure R=Radius h=Wall thickness



Environmental	Stop smoking-1B Physical activity-1B Weight control-1B Chelation therapy-3C Influenza vaccination-1B
/ascular / Tissue	Blood pressure-1B RAAS blockade-1A Aldosterone blockade-1A/B
Metabolics	Lipids-1B Triglycerides-1B Diabetes-1B Antiplatelets-1A/B



Metabolics & Hematology

Lipids-1B

- Fasting lipid profile
- Lifestyle and high fiber
- Omega 3 pills/fish (high triglycerides)
- LDL <100 / 70 (high dose statins ok)
- Targets
 - 30-40% LDL reduction (moderate-high risk)
 - Higher risk 70-100 LDL
 - Very high risk <70 mg/dl -2A
 - Small dense LDL --KILL

Triglycerides-1B

- Triglycerides (200-499)
 - Non HDL <130
 - Niacin / fibrates
- Triglycerides >500 (pancreatitis)
 - Fibrate / niacin before statin
 - Target <130 trig
 - LDL high -combination to get 50% drop
- Diabetes-1B
 - HbA1c <7.0/6.5%
- Antiplatelets-1A/B
 - 75-162 mg ASA for life
 - Coumadin increases bleeding risk
 - Genetic testing for both agents



Insulin Resistant State



Aspirin reduced the risk of first myocardial infarction by 44% (p<0.00001) Physicians Health Study



Thromboxane A₂

Platelets are unable to generate (no nucleus) new cycloxygenase enzyme Endothelial cells also blocked but recovery quickly cycloxygenase

Chilton et al Clinical diabetology March 2011 Mehta et al JACC 2003;41:79s N Engl J Med. *1989 Jul 20*;321(3):183-5

UKPDS 75: Elevated glucose and BP increase MI risk



*Updated mean.

Stratton IM et al. Diabetologia. 2006;49:1761-9.

Additive Effect of Cholesterol and Systolic BP on Risk of CHD Death



Neaton et al. Arch Intern Med. 1992;152:56-64

Lowering LDL with statins reduces CV events



Patients with CHD events (%)

.....Statins work

Statins Reduce Major Coronary Events



>2% per yr-Primary Prevention-Cochrine 2011

Limitations of Statin Monotherapy on CHD Events

			Event	s,* n	Dick		
Trial	Drug	N	Control Group	Statin Group	Risk Reduction, %†	Events not Avoided, %	
4S WOSCOPS CARE AFCAPS LIPID TNT	Simvastatin Pravastatin Pravastatin Lovastatin Pravastatin Atorvastatin	>30,817	2,042	1,490	26	74	
HPS	Simvastatin	20,586	1,212	898	26	74	
PROSPER	Pravastatin	5,804	356	292	19	81	
ASCOT-LLA	Atorvastatin	10,305	154	100	36	64	
Total		67,462	3,764	2,780	27	73	

* Nonfatal MI and CHD death; AFCAPS also included unstable angina † Weighted average

Adapted from Bays H. Expert Rev Cardiovasc Ther 2004;2:89-105.

IVUS and Cardiometabolic Drug Trials



ATHEROMA Trial

- The ATHEROMA (Atorvastatin Therapy: Effects on Reduction of Macrophage Activity) Study
- Forty-seven patients with carotid stenosis >40% on duplex ultrasonography and who demonstrated intraplaque accumulation of IRON oxide USPIO on MRI at baseline

• Double blind

- A-80 mg
- A-10 mg
- 12 week follow up
- Change from baseline in signal intensity on USPIOenhanced MRI in carotid plaque at 6 and 12 weeks

Ultrasmall superparamagnetic iron oxide (USPIO)-enhanced carotid magnetic resonance imaging (MRI)



J Am Coll Cardiol 2009;53:2039–50

Metabolic Syndrome patients with low HDL showed enhanced efflux capacity with pioglitazone...not with statins



Khera et al N Engl J Med 2011;364:127-35

HDL key player in cellular cholesterol efflux



Risk of soft lipid cores

Children-PDAY ↑ BMI more CAD

Atherosclerosis

Normal "looking coronary artery"



Optimal Medical Therapy with or without PCI for Stable Coronary Disease COURAGE

- Stable coronary artery disease with stenosis of at least 70% in at least one proximal epicardial coronary artery and objective evidence of myocardial ischemia
- N=1149 PCI + optimal medical therapy
- N=1138 optimal medical therapy alone
- F/U 2.5 to 7.0 years (median, 4.6)
- Primary outcome (NS)
 - Death from any cause and nonfatal MI
 - 19.0% PCI group
 - 18.5% Medical only
 - Hazard ratio1.05; 95% confidence interval [CI], 0.87 to 1.27; P = 0.62)
- 33% crossed over to PCI
- Levels at end of study
 - LDL-70
 - HDL-42
 - TRG-125
 - BP 122/70



N Engl J Med March 27, 2007;356:000

Moderate-severe ischemia needs blood



Reduction Vascular Events-2011



Percent



HMG-CoA Reductase Inhibitor: Secondary Prevention

Relationship between LDL-C Levels and Event Rates in Secondary Prevention Trials of Patients with Stable CHD



Targets; HPS=Heart Protection Study; CARE=Cholesterol and Recurrent Events Trial; LIPID=Long-term Intervention with Pravastatin in Ischaemic Disease; 4S=Scandinavian Simvastatin Survival Study.

LaRosa et al. *N Engl J Med* 2005;352:1425-1435.



4 take home messages

- Pick your parents carefully
- Control you environment ...drugs / surgery are not match for uncontrolled environment
- Vascular / tissue blood pressure very important..wall stress
- Metabolics nutrients of vascular life...needs clean fuel for healthy endothelium

Acta Physiol 2009, 196, 193–222

Nitric oxide is life





NIRS-IVUS

30 y/o/ Hispanic type 2 DM male A1c 8.5 Obese HDL low High triglycerides Biopsy proven NASH



All laised bill aist arranged

Thank you

