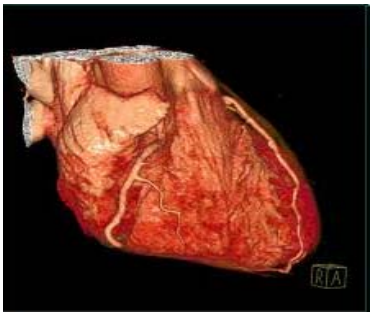
The Management of Chronic Stable Angina



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Objectives

- Understand the pathophysiology of chronic stable angina as well as its symptoms
- Review the evaluation and medical management of chronic stable angina using standard antianginal therapies
- Review emerging antianginal therapies and understand the indication for invasive treatment strategies

Case – Ms. C. Pain

- 56 F with retro-sternal chest pain on effort x3 months
- Hypertensive and dyslipidemic. Non-smoker. Family history ++
- Meds: Lipitor 20 mg po die, Coversyl 4 mg po die.

Is it Angina?

- 3 criteria:
  1. Retrosternal discomfort, usually reproducible
  2. Onset with effort
  3. Ceases with rest (or with NTG)
- Typical angina: 3/3
- “Atypical” chest pain: 2/3
- “Non-anginal” chest pain: 0-1/3

Stable or Unstable?

Stable

- Retrosternal pain reproducible and predictable
- > 3 months
- No change in symptoms

Unstable

- Pain at rest
- Crescendo angina
- New angina (CCS class III-IV)
- Post-revascularisation

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EMERGENCY

Ms. C. Pain

- She feels chest tightness each time she climbs the stairs at work and at home
- ++ Breathlessness. After a short rest, the feeling disappears in 3-5 minutes
- No change in symptoms recently
- No pain at rest

What is the probability that she has obstructive CAD?

Probability of Stable CAD

TABLE I
*Pretest Likelihood for CAD**

Age	Group TA	Group AA	Group NA	Group AS
Males				
60–69	0.943±0.004	0.671±0.013	0.281±0.019	0.123±0.005
50–59	0.920±0.006	0.589±0.015	0.215±0.017	0.097±0.004
40–49	0.873±0.010	0.461±0.018	0.141±0.013	0.055±0.003
30–39	0.697±0.032	0.218±0.024	0.052±0.008	0.019±0.003
Females				
60–69	0.906±0.010	0.544±0.024	0.186±0.019	0.075±0.006
50–59	0.794±0.024	0.324±0.030	0.084±0.012	0.032±0.004
40–49	0.552±0.065	0.133±0.029	0.028±0.007	0.010±0.002
30–39	0.258±0.066	0.042±0.013	0.008±0.003	0.003±0.001

* Each value represents the a priori probability for coronary artery disease (CAD) ±1 standard error. TA, typical angina; AA, atypical angina; NA, nonanginal pain; AS, asymptomatic.

Diamond GA et al. *JACC* 1983

Ms. C. Pain

- Completed 8 mins Bruce protocol. Developed typical angina but stopped test because of fatigue.
- 1 mm depression in V5 and V6. No BP drop. No arrhythmias.
- Hypokinesis of inferior wall and apical anterior segment with exercise. LVEF 50%
- Symptoms and ECG normalise after 2 minutes of rest.

How should she be treated? Does she need PCI?

Summary: Ms. C. Pain

- Typical angina
- Completed 8 minute stress test
- 2-vessel disease (right coronary and distal LAD) based on stress-echo
- Good LVEF

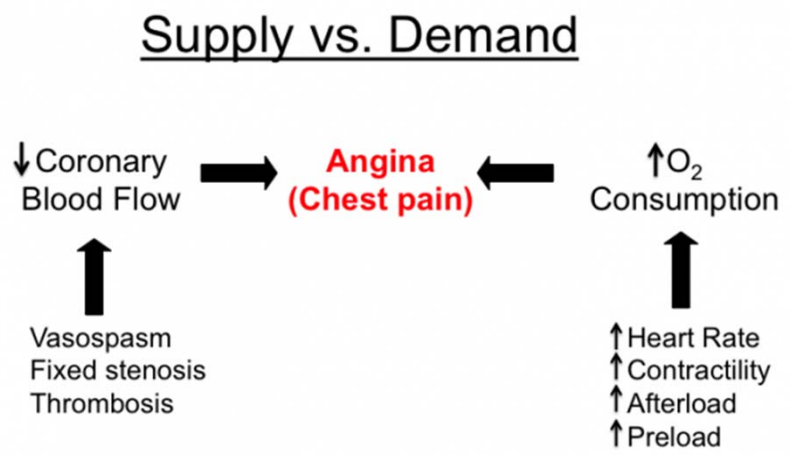
Ms. C. Pain

- Normal examination
- BMI 26 kg/m^2
- BP: 145/85
- LDL 2.8 mmol/L
- Glycemia – normal

Stable CAD Treatment

- Medical
- Revascularisation
  - Percutaneous coronary intervention
  - Bypass surgery

Angina Pathophysiology



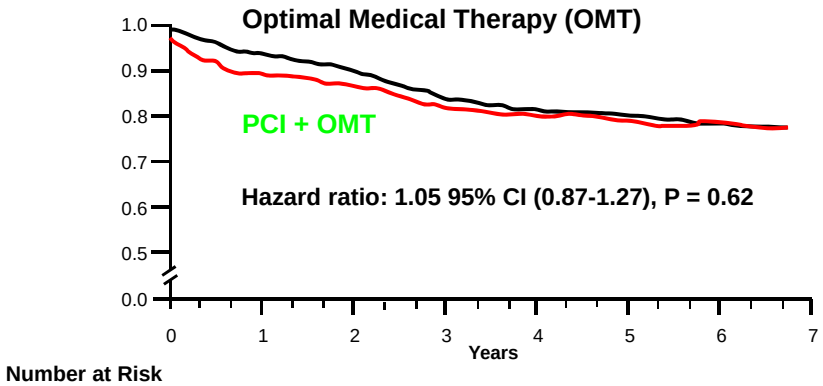
Goals of Treatment

- There are 3 goals in treatment
  - Prevent death and MI
  - Minimise symptoms
  - Slow atherosclerosis progression
- Medical treatment of stable CAD is first line
  - Revascularisation is only for patients at very high-risk

Revascularisation

- Reduces mortality (only if):
  - Left main or equivalent
  - 3-vessel with LVEF <50%
  - 2-vessel (proximal LAD) with LVEF < 50% or large ischemic territory
  - Proximal LAD with LVEF < 50% or large ischemic territory
- Symptomatic control
  - Symptoms refractory to medical treatment (> 2 antianginal agents)

COURAGE Trial – Mortality and MI

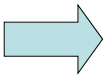


Number at Risk

Medical Therapy	1138	1017	959	834	638	408	192	3
PCI	1149	1013	952	833	637	417	200	3

Lifestyle Modification

- Smoking cessation
- Dietary change
- Increase physical activity
- Cardiometabolic management



Cardiac rehabilitation programme

Medical therapy

Atherosclerosis-modifying drugs

- ECASA (other antiplatelets)
- Statins (ezetimibe and PCSK9i)
- ACE-I (ARBs)
- Icosapent ethyl
- Oral hypoglycemic agents (if diabetes)

Anti-anginal therapies

- Beta-blockers
- Calcium-channel blockers
- Nitrates
- Ranolazine
- Other agents (e.g. nicorandil, trimetazidine)

ECASA

- All patients with stable CAD (unless intolerant/allergic)
- ECASA 81 mg daily
- 33% reduction in vascular events

Statins

- All patients with stable CAD
- Maximally-tolerated dose
- Intensify treatment if LDL ≥ 1.8 on max tolerated dose
  - Consider ezetimibe and/or PCSK9i
- For each 1mmol/L of LDL reduction = 20% mortality reduction

Icosapent ethyl

- Highly-purified eicosapentanoic acid formulation (omega-3 fatty acid)
- Patients with CAD and TGs ≥ 1.5-5.6 mmol/L
- anti-atherosclerosis effect/plaque stabilization
- 25% RRR in CV events
- Dose: IPE 2 grams BID

2021 CCS Dyslipidemia Guidelines

Treatment Intensification Approach for Patients with Atherosclerotic Cardiovascular Disease (ASCVD)

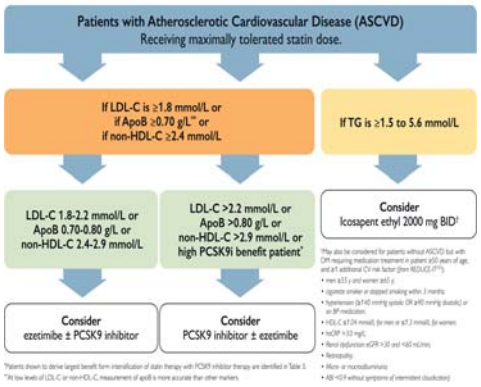


Table 3: Secondary prevention patients shown to derive the largest benefit from intensification of statin therapy with the addition of a PCSK9 inhibitor

Recent acute coronary event (ACS)
• hospitalized index ACS to 52 weeks post index ACS
Clinically evident ASCVD and any of the following:
i. diabetes mellitus or metabolic syndrome
ii. polyvascular disease (vascular disease in ≥2 arterial beds)
iii. symptomatic PAD
iv. recurrent MI
v. MI in the past 2 years
vi. previous CABG surgery
vii. LDL-C ≥ 2.6 mmol/L or heterozygous FH
viii. lipoprotein (a) ≥ 60 mg/dL (120 nmol/L)

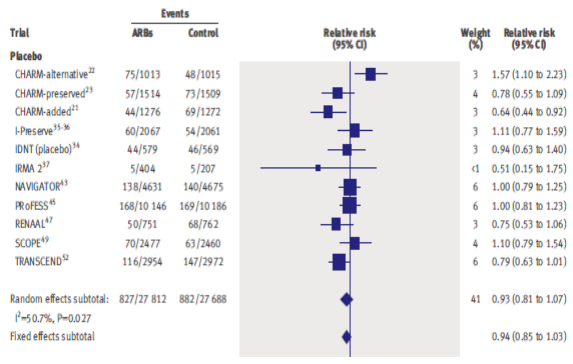
ASCVD = atherosclerotic cardiovascular disease; PAD = peripheral arterial disease; MI = myocardial infarction; CABG = coronary artery bypass graft; LDL-C = low density lipoprotein cholesterol; FH = familial hypercholesterolemia

ACEi

- Reduce BP (target <130/80)
- Little effect on symptoms
- Reduce CV events <u>if HTN, DM2, LVEF < 40% or CKD</u>
  - 14% mortality reduction for select patients
  - Additional effect beyond the antihypertensive effect

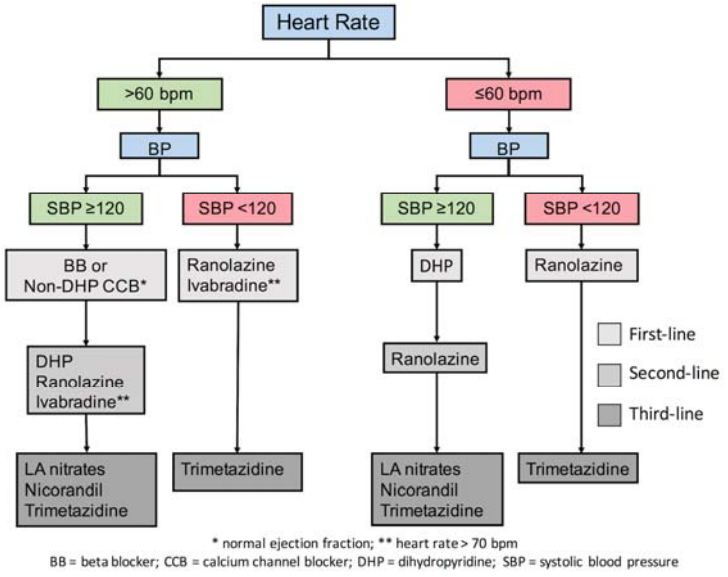
ARB

- Indicated <u>only if ACEi</u> not tolerated
- No MI, CV or all-cause mortality benefit



Trial	Events ARBs	Events Control	Relative risk (95% CI)	Weight (%)	Relative risk (95% CI)
Placebo					
CHARM-alternative[22]	75/1013	48/1015		3	1.57 (1.10 to 2.23)
CHARM-preserved[23]	57/1514	73/1509		4	0.78 (0.55 to 1.09)
CHARM-added[21]	44/1276	69/1272		3	0.64 (0.44 to 0.92)
I-Preserve[35-36]	60/2067	54/2061		3	1.11 (0.77 to 1.59)
IDNT (placebo)[34]	44/579	46/569		3	0.94 (0.63 to 1.40)
IRMA 2[37]	5/404	5/207		<1	0.51 (0.15 to 1.75)
NAVIGATOR[43]	138/4631	140/4675		6	1.00 (0.79 to 1.25)
PRoFESS[45]	168/10 146	169/10 186		6	1.00 (0.81 to 1.23)
RENAAL[47]	50/751	68/762		3	0.75 (0.53 to 1.06)
SCOPE[49]	70/2477	63/2460		4	1.10 (0.79 to 1.54)
TRANSCEND[52]	116/2954	147/2972		6	0.79 (0.63 to 1.01)
Random effects subtotal:	827/27 812	882/27 688		41	0.93 (0.81 to 1.07)
I^2=50.7%, P=0.027					
Fixed effects subtotal					0.94 (0.85 to 1.03)

Anti-anginal treatment



* normal ejection fraction; ** heart rate > 70 bpm

BB = beta blocker; CCB = calcium channel blocker; DHP = dihydropyridine; SBP = systolic blood pressure

Beta-Blockers

- All patients
  - 1st line therapy to <u>reduce symptoms if HR > 60 bpm</u>
  - Reduces mortality (only if)
    - LVEF < 35%
    - History of prior MI (for 1-3 years)

Calcium Channel Blockers

- Non-dihydropiridine CCBs (e.g. diltiazem)
  - Can be used instead of BB as 1st line (only if normal LVEF)
- Dihydropiridine CCBs (e.g. amlodipine)
  - 1st line agent if HR < 60 bpm
  - 2nd line agent to be added to BB therapy for persistent angina
- CCBs only reduce symptoms (no mortality reduction)

Nitrates

- All patients should have a NTG spray
  - Use as needed
  - Use preventively
- Long-acting nitrates (patch or tablets) should be used as a last resort
  - Elderly patients with adequate BP
  - Revascularisation not possible or desired

Ranolazine

- 2nd or 3rd line anti-anginal agent for refractory cases
- Late Na+ channel blocker
- Ranolazine 500 mg bid
- Improves anginal symptoms only

Ivabradine

- Reduces heart rate without drop in blood pressure
- I_f channel inhibitor found in pacemaker cells of the heart
- May reduce angina but may increase CV events
- Not approved in Canada for angina

Conclusions

- Stable angina is a clinical diagnosis
- Stress testing is helpful for diagnosis and prognosis
- Imaging tests can detect patients at high-risk
- Vast majority of stable CAD patients need medical therapy only NOT revascularization
  - Lifestyle change and cardiac rehabilitation programs
  - ASA, BB and/or CCB, statins are first-line

Thank you

Questions?

McGill UNIVERSITY

ARB vs ACE

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Total mortality	8	5201	Risk Ratio (M-H, Fixed, 95% CI)	1.05 [0.91, 1.22]
2 Cardiovascular mortality	4	4131	Risk Ratio (M-H, Fixed, 95% CI)	1.08 [0.91, 1.28]
3 Non-cardiovascular mortality	4	4131	Risk Ratio (M-H, Fixed, 95% CI)	0.94 [0.66, 1.34]
4 MI	2	3874	Risk Ratio (M-H, Fixed, 95% CI)	1.00 [0.62, 1.63]
5 Stroke	1	3152	Risk Ratio (M-H, Fixed, 95% CI)	1.63 [0.77, 3.44]
6 Total hospitalisations	3	4310	Risk Ratio (M-H, Fixed, 95% CI)	1.00 [0.92, 1.08]
7 Hospitalisations for heart failure	3	4310	Risk Ratio (M-H, Fixed, 95% CI)	0.96 [0.83, 1.11]
8 Other hospitalisations	3	4310	Risk Ratio (M-H, Fixed, 95% CI)	1.03 [0.92, 1.15]