Pharmacological Secondary Prevention after AMI – 2022

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NICE 2013, 2020, ESC 2018

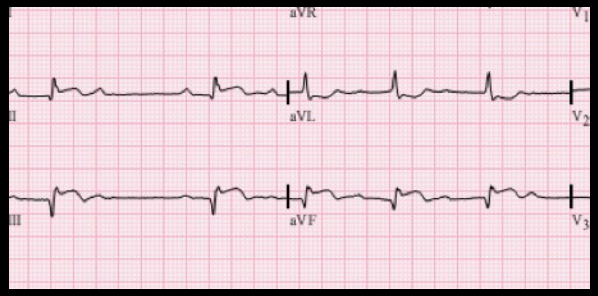
Why?

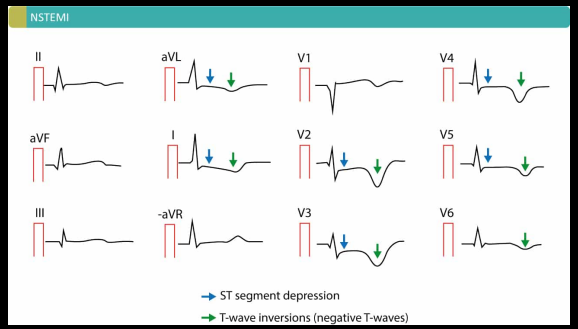
- AMI
-  Recurrence
-  Risk of CVE
- Prolong Life

   Symptoms
- Methods
- Rehabilitation + Lifestyle changes
- Drugs

Statistics

- STEMI
- MR ⇩ from 20% to 5% in 30 y in Hosp
- Incid of hosp adm = 500/mill in UK
  Due to PCI, Pharmacol agents + Rehab
- NSTEMI
- MR remains increased.
- Incid of hosp adm = 3000/mill





Pathology of AMI

- Myocardial Ischaemia - Cell damage.
- Coronary obstruction –Thrombus or Plaque.
- Pre-existing progressive IHD ⟶ Plaques.
- 90% patients who have AMI have IHD (CAD).
- AMI is caused or triggered by many factors.
- RF for AMI/CAD = ///

Trigger factors

RF of AMI /// RF of CAD (IHD)

- Male
- Older
- DM
- HTN
- Hypercholesterolemia
- Smoking
- Past h/o MI

Aims of Treatment of AMI

- ↓ CV Events (AMI, LVD, HF).
- ↓ Symptoms (CP, SOB, Dizziness).
- Improve survival.
- Therefore secondary prevention = Essential.
- Lifestyle intervention (Cardiac Rehab).
- Behaviour change.
  - Smoking, Alcohol.
  - Weight loss if > 25 BMI.
  - Exercise.
  - Diet (Fat, salt, Alcohol).

Pt. Concerns and Clinical Plan

- Return to normal activities – When?
- Before discharge to arrange:

- Assess LV functions.
- Bleeding risks.
- Is PCI necessary now or is planned?
- Cardiac Rehab.
- Behaviour change advice.

Pharmacological Methods

- SAPT, DAPT, TAPT, OAC and Antiplats
- ACEi, ARB
- BB
- Lipid lowering
- Rate-limiting CCB
- Aldosterone blockade
- Antihypertensive
- SGLT2i, GLP-1 Agonists
- Anti-inflammatory therapy
- HF therapy
- ICD

Pharmacological Methods

- SAPT, DAPT, TAPT, OAC and Antiplats
- ACEi, ARB (Entresto)
- BB (carvedilol, bisoprolol, nebivolol, metoprolol)
- Rate-limiting CCB (Verapamil, RLCCB with BB = Contraind)
- Lipid lowering (Reduce LDL-C to <1.4) or add Ezetimibe or monoclonal Ab = Alirocumab) +- Omega 3
- Aldosterone blockade. MRA Spironolactone. When HFrEF
- Antihypertensive (Prioritise BB and ACEi) (120-129, 130-140)
- SGLT2i, GLP-1 Agonists (Empa, Dapa, Canaglifozin)
- Anti-inflammatory therapy (Canakinumab) atheroscler - Colchi
- HF therapy (As above + Ivabradine)
- ICD (Biventricular pacemaker) after 40 days of AMI

SAPT

- Aspirin.
  - Antithrombotic NSAID ↓ Platelet Thromboxane A2
  - Reduces plat-aggreg (which leads to more firm coag – clot).
  - Review in 1994 recommended aspirin and NICE recommends this to be used after AMI ? indefinitely.
  - 75mg Plain, EC, Dispersible – OD, indefinitely.
  - Stabilisation = 2-3d.
  - Offer Aspirin post MI 12 m if not already on it.
- Clopidogrel.
  - Thienopyridine leads to ADP induced platelet aggregation.
  - If intolerant to aspirin then this is second choice.
  - 75mg od, indefinite monotherapy or dual with Ticagrelor or Prasugrel.
  - Duration of effect = 3-10d. Stop pre-op 5d.

DAPT

- DAPT literally means Aspirin and another APA such as:

- Aspirin 75mg + Clopidogrel 75mg.
- Aspirin + Ticagrelor 90mg od (RCT) after AMI.

- Aspirin + Prasugrel (P2Y12 inhib - 10mg od (RCT) after PCI.
- More data now showing aspirin + Prasugrel give better results.
- DAPT should continue for 12 months.
- Can be given with eGFR >15 but dose reduced if eGFR <15.

TAPT or TAT

- With long-term cardiac conditions and AMI, OAC and TAPT. TAPT = Aspirin + Clopidogrel + NOAC.
- Current guidance is after NSTEMI and PCI, OAC + SAPT for 11 months and then lifelong OAC.
- Post AMI usual practice = DAPT for 12 m --- SAPT for life.
- The more you add the more is risk of bleeding.
- NICE does not support antithrombotic therapy for more than 12m but EG says after PCI pts requiring long term therapy TAPT for 6m and then NOAC + SAPT for next 6m and then NOAC indefinitely.
- In UK after MI – DAPT for 12m then SAPT for life.

Renin –Angiotensin –aldosterone blockers (ACEi)

- It blocks AT1 conversion to AT2.
- Increases Na loss and reduces arteriolar resistance.
- Bradykinin increases – May lead to Cough and postural hypot.
- Ramipril, Lisinopril, Fosinopril. SE = K+, Low BP, CKD/ AKI.
- Preliminary UE, LFT, Lipids and BP checks.
- Uptitrate 12-24 hours to max tolerable in 6w.
- UE post treatment or post increase 1-2w.
- If intolerant then use ARBs.
- ACE and ARBs are contraindicated in Pregnancy.
- After AMI and with LVSD, Reduced CV Morb and Mort with ACEi is well known since 30y (HOPE adds DM, PVD as well).
- New gold standard is Entresto instead of ACEi (Paradise trial).

Statin

- Statin = HMG CoA reductase inhibitor. This reduces LDL-C.
- Most useful post AMI regardless of Lipid level.
- After AMI Lipids fall so early basal measurement is needed.
- Reassess after 4-6 weeks. Aim = LDL-C ↓ to <1.14.
- If target not achieved then add Ezetimibe 10-20mg (reduces Intestinal absorp of cholesterol (ImproveIT trial).
- NICE supports Atorvastatin 80mg with LVEDP <40% or HF.
- If target is not reached then consider adding a monoclonal Ab PCSK9 inhibitor = Alirocumab 75-150mg every 2 weeks (Odyssey trial) or evolocumab (Fourier Trial) → ↓ CVE and ↓ CV mort rate).

BB

- Older evidence now superseded by increasing reperfusion.
- Most useful post AMI with LVEDP <40% or HF.
- Aim is to uptitrate to achieve HR 55-60 in Sinus rhythm.

- SE include dose-related Bradycardia, hypotension, fluid retention, fatigue and bronchospasm and cold extremities.
- Not contraindicated in COPD but relatively CI in Asthma.

- Bisoprolol, carvedilol, nebivolol, metoprolol = Cardio selective.
- Use for 12 months if no LVSD. If LVSD + then indefinitely.
- Offer this to pt. without BB post MI 1 year if LVSD present.

CCB – Rate-limiting

- In Post AMI Chronic phase Verapamil 360mg od reduces mortality in the absence of HF (RCT – Danish Trial).
- So if BB are contraindicated then Verapamil is a good choice but when there is no HF.
- Verapamil is contraindicated with a BB.

MRA

- Mineralocorticoid Receptor Antagonist (Aldosterone Antagonist) prevents post-MI remodelling in patients with LVSD.
- These reduce all cause mortality and readmission rate after MI.
- NICE recommends treatment with MRA post MI when there is HFrEF <40% present.
- MRA should be started 3-14 d after MI and after ACEi/ARB.
- Epleronone and Spironolactone are recommended by NICE but European guidelines recommend Epleronone after MI with HF or DM.
- Contraindications of use are renal dysfunction and K++

SGLT2i

- Both SGLT2i and GLP-1 RA (but not DPP4) improve cardiac outcomes after AMI as novel agents.
- SGL2i reduce glucose reabsorption at prox tubules leading to glycosuria and reduced BG level.
- Patients with DM or atherosclerosis post MI show reduced CV events and better outcome.
- Empaglifozin 10 or 25mg, Dapaglifozin 10mg or Canaglifozin 100-300mg) improve cardiac and renal outcome irrespective of glycaemic control.
- SE include intravascular volume depletion and genital infection and DKA (rare).
- In CCF and LVEF <40% (usual picture after AMI) SGLT2i is Reno-protective and cardio-protective.

GLP-1 RAgonist

- GLP-1 RA improve cardiac outcomes after AMI in diabetics.
- GLP-1 RA increase glucose-dependent Insulin and reduce glucagon and increase glycogen synthesis.
- They also improve satiety.
- SE = GIT disturbance (Liraglutide abandonment in Leader trial.
- Another SE was retinopathy with s/c Semaglutide.
- So the Post-MI MR is reduced in Diabetics on SGLT2i and GLP-1 RA.

GLP-1 RAgonist

- Dulaglutide (Trulicity), taken by injection weekly.
- Exenatide extended release (Bydureon), taken by injection weekly.
- Exenatide (Byetta), taken by injection twice daily.
- Semaglutide (Ozempic), taken by injection weekly.
- Semaglutide (Rybelsus), taken by mouth once daily.

ICD

- Most patients develop LVSD after AMI therefore further treatment will be salvage in patients after AMI with EF >35%:
- Ivabradine.
- Cardiac resynchronisation (biventricular pacemaker).
- Biventricular defibrillator.
- ICD should be implanted after 40d of MI.