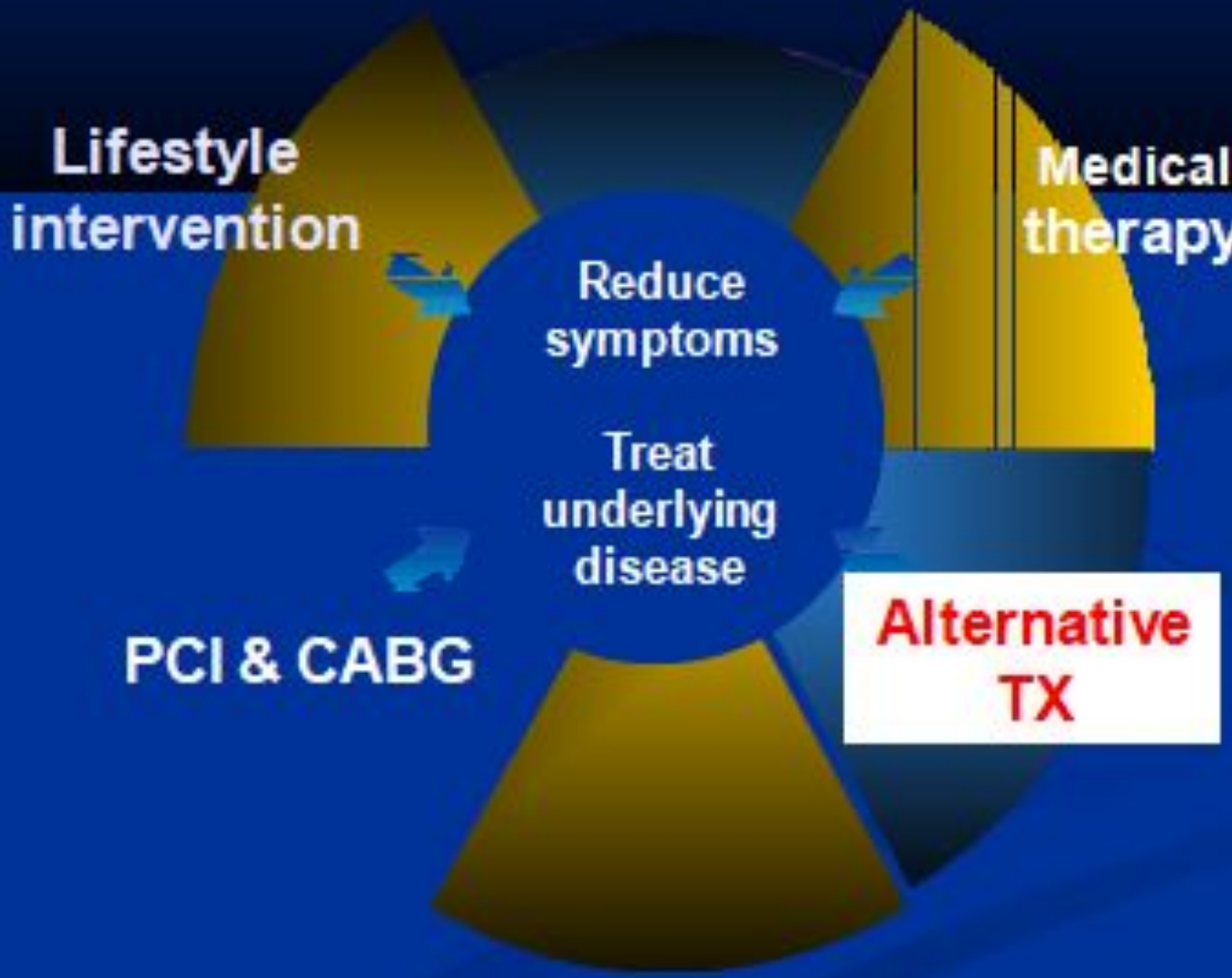
Refractory angina and unrevasculrizable patients with CAD

By
Prof. Mazin Zamel ALshibani

CAD: Multiple treatment options



Review of Conventional Medical Therapy Commonly used for IHD

BB-decrease heart rate and contractility *

CCB-act as arterial vasodilator and decrease heart rate and * .contractility

Nitrates-act as veno-arterial vasodilator *•

Antiplatelet agents-for anti-inflammatory activity *•

* ACEIs & ARBs-improve endothelial function, and for anti-inflammatory activity

* Statins-improve endothelial function, anti-inflammatory activity and lipid lowering agents

Chronic ischemic heart disease: Treatment gaps

- Many patients have relative intolerances to maximum doses of traditional antianginal agents)β-blockers, CCBs, and nitrates

- Patients continue to experience myocardial ischemia
- β-blockers and many CCBs have similar depressive hemodynamic and electrophysiologic effects

- Recurrent angina after PCI: 15-20 % at 2 ys,
  after CABG: 10 % at 1y
- Repeat revascularization after PCI: 10-20 % at 2 ys,
  after CABG: 25 % at 2 ys

The magnitude of the problem

- A significant number of patients *(5–21%)* with ischemic heart disease are not optimal candidates for revascularization (PCI/CABG) or receive incomplete revascularizations with these procedures.

- Many of them have residual angina and congestive heart failure symptoms despite maximal medical therapy. Thus an alternative treatment strategy is needed

Refractory angina

- Defined by presence of severe angina with objective evidence of ischemia as demonstrated by TMT, stress imaging studies or coronary physiologic studies and failure to relieve symptoms with conventional medical therapy and even with revascularization techniques.

- Patients with refractory angina have either marked limitation of ordinary physical activity or are unable to perform any ordinary physical activity without discomfort or pain at rest (CCS class III or IV).

- Periodic assessment is mandatory, and patient may amenable for revascularization at any time.

What is Refractory Angina?

- *CCS class III-IV Angina*
- *Duration of more than 3 months.*
- *CAD*
- *Objective evidence of reversible myocardial ischemia*
- *On medical therapy*
- *Not suitable for PCI or CABG*

Why Patients are Inappropriate for Revascularization ?

- Location of the stenosis (e.g. graft stenosis), distal stenosis, multiple stenoses or a combination of these three factors
- Potential risk of damaging pre-existing grafts.
- Often, the reason for rejection was a combination of these two factors.
- High risk patients with regard to both CABG and PCI due to comorbidites, old age and/or coronary anatomy are unsuitable for revascularization
- Lack of graft, unsuitable anatomy, diffuse sclerotic changes, and impaired LV function in patients with previous PCI or CABG

Alternative theraputic options for refractory angina

A. Pharmacological (ranolazin, trimetazidin, nicorandil, ivabradin, fasudil)

B. Nonpharmacological:

1. EECP
2. TMR
3. Chelation therapy
4. SCS
5. CSO or reducer
6. Gene therapy
7. Coronary venous arterialization
8. Heart transplantation

Medical treatment

- ***Trimetazidine***...*metabolic agent, ↑metabolic efficiency of myocyte,(–) F.A metabolism, (+) glucose metobolim, ↑coronary blood flow.*

- ***Ranolizine***... *peprazine derivative, shift metabolism of myocyte from FA to glucose, unique anti-ischemic effect, no effect on HR & BP.*

- ***Ivabradine***...*selective effect of conduction system, slow HR during peak exercise. Shift pt from ↑risk - ↓risk , ↓MI, no –ve inotropic (**Heart rate above 70 increases risk of coronary revascularization by 38%**)*
- ***Nicorandil***....*k channel activator, dual action ↓preload & afterload.*
- ***Fasudil***... *Rho- kinase inhibitor and vasodilator*

How does trimetazidine work?

- Anginal patients accumulate FFAs, which the cardiac muscles oxidise for their energy requirements,
- LCFA oxidation demands more ATP to break down the FFAs than glucose oxidation.
- This demands more O2 and more blood supply from the anginal heart, adding to the load on the compromised heart.
- This is prevented by trimetazidine which shifts metabolism from LCFAs to glucose.

Ranolazin

* Renexa 500 mg (500mg x2 and increase to 1000 mg x2), should be giving with BB, amlodipin or nitrate.

* It improve survival rate, increase exercise ability and anginal free period and improve HbA1c that improve physical activity and increasing insulin sensitivity)

* It is a partial inhibitor of fatty acid oxidation.
* Prolong QT interval
* Reduction of digoxin, antipsychotic, tricyclic antidepresant and simvastatin dose when used with ranolizin

Understanding Fasudil

- Fasudil Hydrochloride is a potent Rho-kinase inhibitor and vasodilator. Rho-kinase proteins are involved in a variety of biochemical signalling in the cells..
- Fasudil is used for cerebral vasospasm treatment , as well as to improve the memory decline seen in stroke victims and in Alzheimer's pts.

Understanding Fasudil in CAD

- Increased activity of Rho-kinase causes hypercontraction of vascular smooth muscle
  - This has been implicated as playing a pathogenetic role in divergent cardiovascular diseases such as coronary artery spasm.
- Inhibition of Rho-kinase helps blood vessels to relax and increases the blood supply of cardiac tissue.
- This forms the basis of use in CAD, but spasm is not always present in CAD.

EECP -Enhanced External CounterPulsation

- It is a non invasive outpatient therapy consisting of ECG-gated sequential leg compression.
- External, pneumatic compression of lower extremities in diastole.

- 35 hrs total time of treatment
- 5 days per week x 7 weeks
- 1-2 hour per day

Contraindications & Precautions

- Arrhythmias that interfere with machine triggering
- Bleeding diathesis
- Active thrombophlebitis & severe lower extremity vaso-occlusive disease
- Presence of significant AAA(5 mm) or dissection
- Pregnancy
- Decompensated heart failure
- Severe aortic regurgitation
- Severe hypertension: greater than 180/ 110mm Hg
- Severe chronic obstructive pulmonary disease

Side effects

- Paresthesias
  - Skin abrasion or ecchymoses
  - Bruises
  - Worsening of heart failure in patients with arrhythmias
  - Leg or waist pain,
- Oedema

Transmyocardial laser revascularization(TMR)

Utilizes a laser to create channels within the myocardium either via the surgical epicardial approach or percutaneous endocardial approach.

It was originally proposed that myocardial perfusion could be achieved by the creation of transmyocardial channels, which communicate with the left ventricular cavity, thus mimicking the physiology of blood flow in normal hearts

Patients with poor LV EF are not good candidate for TMR

Neurostimulation

- For the palliation of angina by interruption or modification of the afferent signals.

- More recent studies using transcutaneous electrical nerve stimulation (TENS) and spinal cord stimulation (SCS)

- They act by *reducing the activation of central pain receptors.* In addition, there is a reduction in sympathetic discharge, leading to a decrease in cardiac work load and myocardial oxygen demand.

Contraindications to this therapy include

- Unstable angina
  - Unfavorable physical condition
  - Cardiac pacemaker or ICD
  - Lack of patient compliance
- Obvious infection, allergic or immune response to implanted materials
  - Anticoagulation that might increase bleeding at the implantation site.

Gene therapy

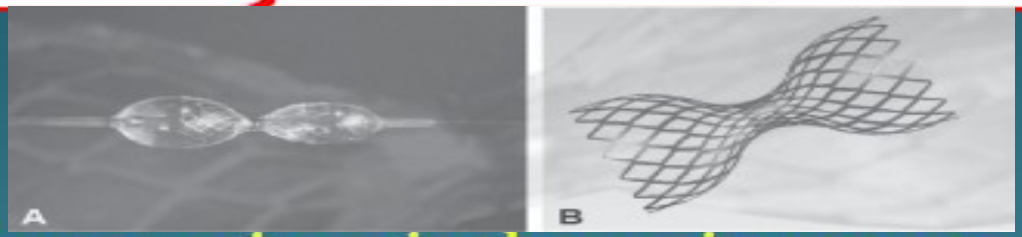
** Genes encoding (protein) growth factors to enhance myocardial angiogenesis primarily involves vascular endothelial growth factor (VEGF)and fibroblast growth factor (FGF) with multiple delivery methods (intravenous, intracoronary, intramyocardial).

**Vasculogenesis: formation of new vascular structures from stem cells during emberyogenesis and may contribute to adult neovascularization.

**Angiogenesis: formation of thin-walled endothelium lined structures lacking smooth muscle layer.

**Arteriogenesis: formation of vessels with a complete smooth muscle

Coronary Sinus Occlusion



- The coronary sinus is the main venous structure that drains blood away from the heart

- By occluding this conduit, lead to redistributing the blood already in the coronary system into relatively underperfused, ischemic territories.

- Creates controlled narrowing to modulate flow and elevate CS pressure which increases endocardial perfusion providing relief of ischemia

Percutaneous in Situ Coronary Venous Arterialization

- PICVA is a percutaneous approach that redirects arterial blood flow from the occluded artery into an adjacent coronary vein then redirected back to the artery after the lesion, thereby arterializing the vein and providing retroperfusion to ischemic myocardium.

- Even in the most severe cases of CAD, the venous system is generally free of atherosclerosis.


THANK YOU