Antiplatelet Therapy

STEMI and Reperfusion Therapy

In management of STEMI, time to treatment is critical. PCI is always better than thrombolytic therapy. According to ACC/AHA guidelines, door to balloon time for PCI should be less than 120 minutes. However, according to data from MITI trial if the patient is seen within 70 minutes of onset of symptoms, prehospital fibrinolytic therapy is very useful and is associated with better outcomes. Even if the patient is seen within 120 minutes, fibrinolytic should be given before transferring the patient to a PCI centre. If the patient is seen later than 120 minutes he should be loaded with clopidogrel and transferred for primary PCI.

SCD and IHD- Global and Indian Perspective

Sudden cardiac death and ischemic heart disease have an enigmatic relationship. IHD is the most common cause of SCD. We have data from very few countries like those in North America and Europe. The challenge in the Indian scenario is that the data are not reliable. Globally the burden of SCD is 5.6% of all deaths while in India it is 10% of all deaths, which is a sizable number. Also, while the mean age of patients of SCD is 74 years globally, in Indians most of the SCDs occur in a much younger age group (50-70 years), the mean age being 60 years. Additionally, majority of SCDs in Indians occurred in hypertensives, diabetics and smokers. To tackle the problem of SCD in India, which is facing an epidemic of diabetes and CAD, we need to screen and treat people for coronary risk factors, treat ACS timely with timely revascularisation, ensure compliance with proper medication (ACEIs, statins, aspirin, etc.) and identify patients at high risk and provide them with ICDs.

State of The Art

Antiplatelet Therapy in ACS

- FDA boxed warning on clopidogrel: Diminished effectiveness in poor metabolizers.
- Prasugrel: More efficiently metabolized, more potent, more rapid onset of action than clopidogrel.
- TRITON TIMI-38: Prasugrel more superior to clopidogrel, significant reduction in CV deaths but at the risk of more bleeding; net clinical benefit was in favor of prasugrel; dramatic reduction in stent thrombosis.
- Ticagrelor: Faster, greater & more consistent platelet inhibition; potential advantage if needing to stop therapy due to surgery as reversible. Ability of platelet function to recover faster vs clopidogrel.

Diligent attention should be paid to history, physical examination for ECG. Also vital is screening at 12-14 years of age and periodic updates.

Yukon® Choice PC

Sirolimus Eluting Coronary Stent System

- Yukon® Choice PC has microporous surface which enables minimal load of biodegradable polymer for optimizing the release kinetics (less polymeric load compared to other DES).
- Yukon® Choice PC becomes a polymer free stent as the polymer gets degraded as soon all the drug is released in 90 days.
- In ISAR Test 4, a trial involving more than 2600 patients Yukon® Choice PC proves non-inferiority to Xience and Cypher in terms of late loss, binary restenosis TLR and primary composite MACE* despite having minimal polymer load.

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Cardiology Medialab

The essential components of negligence as recognised are three: “duty”, “breach” and “resulting damage”
Unprotected LMCA Stenting
Follow up Surveillance Angiography

No consensus on necessity and timing. Angiography follow-up timing should be 3-4 months. If early angiography reveals patent stent perform stress testing at 6-9 months. If angiographic restenosis is observed:
- In LM artery: If occurs early and is severe then consider CABG & if it occurs late and is moderate, then consider PTCA.
- In ostial LAD/LCX, IVUS/FFR to confirm physiologic significance (asymptomatic). If restenosis involve both ostia: Consider CABG. If restenosis involves one ostium: PTCA.
- Offer LM PCI to patients at high risk for surgery due to comorbidities, suboptimal distal targets and if the patient cannot get a LIMA to the LAD.
- Offer PCI if the patient does not fulfill the above & refuses CABG with the following caveats: Do not perform ad hoc LM stenting. During informed consent emphasize CABG as the traditional approach and ask a cardiac surgeon to speak to the patient.
- Ensure that the patient commits to long-term antiplatelets and short-term surveillance angiography.

Corrigendum: This story was erroneously published yesterday. The corrected story is carried today. We sincerely regret the error.
How to Explain Cardiac Interventions to Your Patients?

This is what I tell my patients. Following are the options to manage any traffic:

- Placing traffic signals, which can be equated to Do’s and Don’ts of lifestyle management.
- Posting a traffic inspector on the crossing. This can be equated to a clinical cardiologist.
- Diverting the traffic from main road to side roads. This can be equated to opening collaterals by drugs, exercise.
- Hiring the architect to draw a blueprint. This can be likened to an angiographer doing angiography.
- Looking for the possibility of widening the roads. This is balloon angioplasty.
- To prevent encroachment of widened roads to place rallying around the widened roads can be equated to placement of metallic stent.
- To prevent rallying from mishandling, grills are put on the rallying. This can be equated to drug-eluting stents.
- When the roads cannot be widened, flyovers are made. This is bypass surgery.
- Flyovers can be made by stopping the traffic. This can be equated to open bypass surgery.
- Flyovers can be made without disturbing the traffic. This is heart bypass surgery.

Advances that Have Changed Cardiology Practice In 2012

Antithrombotic therapy for patients with atrial fibrillation: An oral direct thrombin inhibitor or a factor Xa inhibitor should be preferred over warfarin in patients with atrial fibrillation (AF) in whom anti-coagulant therapy is indicated. In 2010, the US FDA approved the use of dabigatran for patients with AF who are at risk for stroke.


Eelective, nonelective surgery in prosthetic mechanical valve. No guidelines available. We are overseeing heparins after stopping warfarin for non cardiac surgery. In low risk procedures, stop warfarin for three days, do the procedure, restart on day 5. Only in high risk patients for PTE patients, switch to heparins during the period of surgery. In emergency surgery, give vitamin K, and perform the surgery.

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Spontaneous coronary artery dissection

A single-center report from the Mayo Clinic of 87 patients who presented over three decades concluded SCAD affects a young, predominantly female population, frequently presenting as STEMI. Spontaneous coronary artery dissection should be considered in the differential diagnosis of any young woman who presents with acute MI, particularly if traditional risk factors for coronary heart disease are absent.


Mitrval valve surgery at the time of CABG

Adding mitral valve repair to CABG in patients with left ventricular dysfunction and moderate to severe MR may improve survival compared with CABG alone or medical therapy alone.


Timing of surgery for native valve endocarditis

Early surgery (within 48 hours of randomization) in patients with infective endocarditis and large vegetations significantly reduced the composite end point of death from any cause and embolic events by effectively decreasing the risk of systemic embolism as compared with conventional treatment (surgery during the initial hospitalization/during follow-up).


(Contd. on next page)
Endoscopic vs open vein-graft harvesting for CABG
Among patients undergoing CABG surgery, the use of endoscopic vein-graft harvesting compared with open vein-graft harvesting was not associated with increased mortality. Williams JB, et al. JAMA 2012; 308(1):475-4.

Vorapaxar in stable CVD
In the TRA 2P-TIMI 50 trial of patients with stable cardiovascular disease who were receiving standard therapy, inhibition of PAR-1 with vorapaxar reduced the risk of cardiovascular death or ischemic events. However, it increased the risk of moderate or severe bleeding, including intracranial hemorrhage. Morrow DA, et al. N Engl J Med 2012;366(15):1404-13.

Prognostic significance of right precordial T-wave inversion
T-wave inversions in right precordial leads are relatively rare in the general population, and are not associated with adverse outcome. Increased mortality risk associated with inverted T waves in other leads may reflect the presence of an underlying structural heart disease. Murad AL, et al. Circulation 2012;125(21):2572-7.

Coronary CT angiography

TAVR vs medical therapy
TAVR reduced the rates of death and hospitalization, with a decrease in symptoms and an improvement in valve hemodynamics that were sustained for 2 years of follow-up among appropriately selected patients with inoperable severe AS. Extensive coexisting conditions may reduce the survival benefit of TAVR. Makkar RR, et al. N Engl J Med 2012;366(18):1696-704.

TA EV vs surgical therapy
In a 2-year follow-up of patients in the PARTNER trial, the two treatments were similar with respect to mortality, reduction in symptoms, and improved valve hemodynamics, but paravalvular regurgitation was more frequent after TAVR and was associated with increased late mortality. Kodali SK, et al. N Engl J Med 2012;366(18):1686-9.

Risk of major bleeding with aspirin
In a population-based cohort of almost 200,000 Italian citizens, aspirin use was significantly associated with an increased risk of major gastrointestinal or cerebral bleeding episodes compared to aspirin non-users (5.6 versus 3.6 per 1000 person-years). Patients with diabetes had a high rate of bleeding that was not independently associated with aspirin use. De Berardis G, et al. JAMA 2012;307(21):2269-94.

Cardiology Medilaw
If the complaint filed is not within the defined prescribed manner, it stands to be rejected.
AHA 2012 Highlights

Low platelet reactivity does not affect outcomes in ACS: Among patients with ACS without ST-segment elevation and initially managed without revascularization, prasugrel was associated with lower platelet reactivity than clopidogrel, regardless of dose. No significant differences were observed as regards the occurrence of the primary efficacy endpoint between prasugrel vs clopidogrel in the platelet-substudy through 30 months. A lower platelet reactivity with prasugrel vs clopidogrel has no impact on ischemic outcomes.


Ultrasound unsuccessful acute HF: The use of a stepped pharmacologic (diuretic)-therapy algorithm was superior to ultrasound for the preservation of renal function at 96 hours in patients with acute decompensated heart failure with cardiorenal syndrome. The weight loss was similar with the two strategies. Ultrasound was associated with a higher rate of adverse events.


Monitoring to adjust antiplatelet therapy for stenting of no use: The ARCTIC trial showed no significant improvements in clinical outcomes with platelet-function monitoring and treatment adjustment for coronary stenting, as compared with standard antiplatelet therapy without monitoring. The study data do not support the routine use of platelet-function testing in patients undergoing coronary stenting.


Cardiac re-arrrest increases chances of death: Patients who experienced even transient loss of pulses prior to hospital arrival after the successful return of spontaneous circulation were more likely to have an unfavorable outcome. Patients who had unresolved prehospital re-arrrest after an out-of-hospital cardiac arrest had greater than six-fold odds of death prior to hospital discharge. Survival rate was 7.8% among cases of unresolved pre-hospital re-arrrest as compared to 33.3% in cases without.

Salcedo DD, et al. AHA 2012; Abstract 68.

Dalteparin increases HDL but has no impact on CV events: In a phase III trial in patients with recent ACS, dalteparin, the CETP inhibitor significantly increased HDL but had no effect on outcomes.

The combined risk of death from heart disease, nonfatal MI, ischemic stroke, hospitalization for unstable angina, and re-suscitated cardiac arrest wasn’t any lower than with placebo.


A novel drug for heart failure: Treatment of acute heart failure with serelaxin (recombinant human relaxin-2), is a vasoactive peptide hormone relieved dyspnea and improved other clinical outcomes, but did not affect hospital readmission rates in the RELAX-AHF (RELAXin in Acute Heart Failure) trial. Serelaxin treatment was well tolerated and safe, supported by the reduced 180-day mortality.


Blood group may predict risk of stroke: If your blood group is AB, then you are at greater risk of stroke. In two cohorts with more than two million person-years of follow-up, individuals in the AB blood group were at a significantly increased (25%) risk of developing stroke than those with type O blood group. Women with type B blood group had a slightly significant 15% higher risk of stroke compared to women with type O blood group.

Qi L, et al. AHA 2011; Abstract 1688.

Polypill strategy improves adherence to therapy: A fixed-dose combination pill (aspirin + a statin + 2 antihypertensives) improved adherence to medications for secondary prevention in patients with or at high risk for cardiovascular disease in the Use of a Multidrug Pill In Reducing Cardiovascular Events' (UMPRIRE). At 15 months, more patients in the polypill group were adherent than those who continued with usual care; 86% vs 65%, respectively (a relative 33% increase).


Low dose aspirin fails to prevent recurrent VTE: Compared with placebo, aspirin did not significantly reduce the rate of recurrence of venous thromboembolism in patients with a first unprovoked event but significantly reduced major vascular events (VTE, myocardial infarction, stroke, or cardiovascular death) in the ASPIRE trial.

Decade of Evolution of Drug-eluting Stents: From Histopath lab to Cath Lab

- First-generation drug-eluting stents (DES) have dramatically reduced restenosis as compared to bare metal stents (BMS); however, this comes at the price of increased risk of late and very late stent thrombosis (LST/VLST).
- Pathologic studies have demonstrated that delayed arterial healing characterized by poor endothelialization is the primary substrate responsible for LST/VLST following DES placement, which is associated with stent struts penetrated into the necrotic core (acute myocardial infarction [AMI] indication), hypersensitivity reaction (sirolimus-eluting stents [SES]) and malapposition (SES and paclitaxel-eluting stents [PES]).
- Second-generation zotarolimus- (ZES) and everolimus-eluting stents (EES) show significantly less uncovered struts with lower incidence of LST as compared to 1st-generation DES. However, stent fracture, neothrombosis, and late catch-up phenomenon (restenosis) are still important issues in second-generation DES.
- Both biodegradable polymer DES and polymer-free drug-coated stent have shown promising results in animal models with significant reduction in neointimal growth similar to permanent polymer DES, with less inflammation and faster healing.
- Bioabsorbable scaffold showed promising results in preclinical studies with almost full degradation at 2-3 years in porcine and rabbit model, and complete degradation at 4 years, although the indication in human is yet to be limited.

Management of Acute IHD in 2012
Have We Reached the Limits?

- Higher sensitivity troponin can identify previously missed individuals with non-STEMI, and the potential for benefit.
- Risk scores are needed to accurately identify those for invasive therapy (evidence from NICE and GRACE programme).
- Novel imaging approaches can identify plaques and plaque inflammation.
- Most MIs and deaths occur in the longer follow-up after non-STE MI and novel treatments are needed to reduce these complications (on top of current evidence based therapy).
- Applying evidence based therapy on a national scale (MINAP UK Programme) has resulted in striking improvements in deaths and MIs (40% decline in cardiovascular deaths in 10 years).

AHA 2012 Highlights

Colchicine safely and effectively prevents postop Afib: Colchicine reduced post operative atrial fibrilalation by 42.1% compared to placebo with shorter in-hospital and rehabiliation stay, according to the results of the COPPS POAF substudy.


Increasing clopidogrel dose may be the answer: In patients with stable cardiovascular disease, tripling the maintenance dose of clopidogrel to 225 mg daily in CYP2C19*2 heterozygotes achieved levels of platelet reactivity similar to that seen with the standard 75-mg dose in noncarriers; in contrast, for CYP2C19*2 homozygotes, doses as high as 300 mg daily did not result in comparable degrees of platelet inhibition.

U Shaped Curves in Heart Failure

A “U-shaped curve” denotes a non-linear association of a factor or variable with a specific outcome. Classical examples of a “U-shaped curve” in medicine includes the effect of alcohol consumption on CV outcomes or the effects of diabetic control on CV outcomes where both hypoglycemia (too much control) and persistent hyperglycemia (too high HbA1c) are bad. There are distinct “U-shaped” curves in HF including but not limited to:

- Neurohormonal therapy “ceiling effect”: Some neurohormonal drugs reduce mortality and modify disease state while excess stack on therapy worsens survival.
- Obesity “paradox”: Though obesity predisposes to more and earlier development of heart failure, patients with obesity tend to have a survival benefit compared with those HF patients without it.
- “Failed” lipid therapy paradigm: The lower the cholesterol, the worse is the prognosis of HF patients. Also, therapy with statins is favorable in all situations of CVD except that in HF there is no clear benefit noted.
- “Uncertain” Hb target effects: The outcome is worse in HF patients with very low and very high Hb. Also, therapy to treat anemia in HF is associated with variable effects, and can sometimes be harmful.
- HF is a condition where too little or too much of a thing are clearly bad: one must get it “just right”.

Growing Indications for Dysrhythmia Management

There are several major areas in which cardiac arrhythmias have major public health importance in diverse populations throughout the world. AF affects 5% of patients >65 years of age, and 10% of patients >75 years old. Recent developments are altering our approach to these patients, including apparently contradictory trends. We are using less antiarrhythmic drugs to suppress AF, and more rate control in selected individuals. On the other hand, we are using more invasive approaches with catheter ablation instead of antiarrhythmic drugs. Trials are underway to evaluate preference of these approaches. In the area of sudden death, while ICDs are the primary therapy for high-risk individuals, this therapy is expensive and has risks. Multiple studies are evaluating more precise methods to determine which patients are most likely to benefit from this therapy. Non-traditional antiarrhythmic therapies: spinal cord stimulation to treat HF and ventricular arrhythmias, as well as CRT to both treat patients with advanced HF and prevent progression. Molecular therapies are being investigated to substitute patients with advanced HF and prevent progression. A public health awareness program was also held. The delegates and accompanying persons enjoyed the entertaining cultural programme by noted Bollywood singer Shaan.

Expectations & Implications from JNC 8

The following are my views and not on behalf of JNC. JNC 8 is delayed again … will be released in mid-2013—finally!! New guidelines will provide revised approach on BB in HT; older BBs like atenolol will be deemphasized. Newer BBs like nebivolol will get special attention. Diuretics will also be reassessed in JNC 8. It is likely that chlorthalidone may get special mention over HCTZ. Superggressive treatment of HT in diabetics is not helpful (ACCORD). So, for a hypertensive diabetic, the goal will be same as before (130/80) but not any lower. Superaggressive treatment of HT in diabetics is not helpful (ACCORD). So, for a hypertensive diabetic, the goal will be same as before (130/80) but not any lower.

Management of Endocarditis

- There is no “cookbook” approach to proper therapy for infective endocarditis, especially when considering surgery.
- In selected patients, combined medical and surgical therapy offers substantial benefit vs medical therapy alone.
- Final outcome has never been related to duration and intensity of prior antibiotic treatment; surgery should not be delayed when clearly indicated in the vain hope that a sterile operative field can be achieved.
- IE surgery carries significant risk and decision on whether or not to operate must be carefully thought out with good communication between surgical and medical teams.

Pharmacoinvasive strategy is the choice of Rx for STEMI management in India. Shortage of cath labs & interventional cardiologists prevents use of primary PCI as primary management strategy.

Renal denervation therapy may play a key role for reducing cardiovascular mortality in future. SIMPLICITY II trial results are very encouraging.

Dr Subroto Mandal

A Message From the Organizing Secretary

Dr Buxton

Dr Rakesh Chopra

Dr C Venkata S Ram

Dr MS Mehra

Dr Alfred Buxton

Dr John G Harold

The 64th annual conference of CSI and SAARC Cardiac Congress 2012 was really an academic feast par excellence. We all enjoy reading the gist in the daily conference newsletter.

Cardiology Medilaw

BOOK RELEASE

LEADERS a foundation for the future
New Antiplatelet Therapy in ACS Aligning Evidence to Practice

In a very lucid talk Dr Chandra began by pointing out the complex nature of the small but very significant platelet cell and stressed that it was due to this complex structure of multiple receptors that we are unable to find the perfect agent to conquer it.

There is no agent that can specifically target platelets. Aspirin is the most approved antiplatelet drug. The best dose is 75-100 mg daily. Adding different antiplatelet agents enhances its efficacy. Clopidogrel though a very good drug showed variable response in different patients causing it to be unpredictable.

Prasugrel is better and more reliable for platelet inhibition and controlling death, MI and stroke. But the risk of bleeding was more and it needs to be stopped 7 days before CABG. Ticagrelor showed decreased incidence of stent thrombosis and bleeding episodes as also decrease in death, MI and stroke. It can also be used in both PCI and non-PCI patients.

Hence, aspirin should be given to all patients unless C1; clopidogrel remains drug of choice if bleeding risk is high. Prasugrel and Ticagrelor are very good options.

Secondary Prevention of CAD by Interference with RAS

ARBs are not just ACEI without the cough & cough is not always deleterious opined Dr Ferrari very passionately! According to him cough is a protective mechanism and decreases the incidence of pneumonia with use of ACEI use.

This discourages the discontinuing of ACEI in those patients who can tolerate cough. The goal of HT treatment is to decrease BP and the risk of cardiac mortality. ACEI and ARBs are both equally effective in reducing BP. ACEI are better than ARBs in CAD in decreasing mortality. If the medical community continues to ignore this evidence and prescribes ARBs over ACEI for HT then the benefit of ACEI will be lost.

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Approach to Manage HT as in JNC is Desirable but not Feasible in India

- In people >50, SBP is more important than DBP as a CVD risk factor. With each increment of 10/20 mmHg, CVD risk doubles.
- Health promoting lifestyle is applicable to all adults & even children.
- ABPM is expensive & its widespread use in India is not feasible; HBPM is also expensive and difficult due to high illiteracy levels.
- Branding as preHT may jeopardize a person’s QOL.
- Pre Rx tests are not possible in India so treatment should be started without them.
- Most Indian men and women are physically inactive, eat high fat diets, this means changing the habits of half of the population.
- Thiazides should be used with caution: hypotension (climate), DM, dyslipidemia, hyperuricemia may worsen with diuretics.
- BB should be used with caution due to high prevalence of DM & dyslipidemia.
- ACEIs and ARBs are expensive.