Heartbeat Highlights from 2003

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Throughout 2003, *Heartbeat* has reviewed a number of important studies and topics. In this issue we will summarize the important conclusions from *2003 Heartbeats* with clinical implications that can be applied to your practice when appropriate in 2004.

HBP: Controlling BP to less than 130/80 is paramount. We agree with the aggressive new JNC VII guidelines that lowering BP toward the new goal level of 120/80 will decrease heart attacks, HF, stroke, kidney disease, and will save lives. Start TLC in pre-hypertension (>120/80).

Two large anti-hypertensive studies (ALLHAT & ANBP2) came to different conclusions about optimum BP treatment. ALLHAT concluded that diuretics were best, but the Second Australian National Blood Pressure Study (ANBP2) demonstrated the superiority of ACE inhibitors over diuretics as first-line therapy in elderly hypertensive patients. Based on the results of ALLHAT and ANBP2 and many other studies it appears obvious that ***both*** diuretics and ACE inhibitors are extremely effective in lowering blood pressure and improving clinical outcomes. Furthermore, both studies showed it was frequently necessary to prescribe a second or third medication to reach adequate blood pressure goals. *Treatment of essential hypertension in African-Americans patients (ALLHAT) should probably begin with a diuretic, with the addition of an ACE inhibitor if needed. For Caucasian patients (ANBP2), the reverse order is appropriate.*

Although population-based studies help point the way, they are not analogous to the care of individual patients. Treatment is complicated, requiring time, judgment and adjustment based on each individual patient's clinical history and response (Table 1). Given the need for more intensive CV and renal risk reduction, we need strategies to simplify our approach to BP reduction. Combining drugs is key. *The combination that gets the best clinical outcomes seems to be a diuretic and an ACE inhibitor, using generics for the least cost and ARB/diuretic if ACE is not tolerated.* This will be the preferred first-line means of decreasing risk and BP. Adding other drugs will probably be necessary to get to goal blood pressure.

Table 1. Treatment of Hypertension 2004

Co morbid Condition	Indicated Drugs*
Heart failure	ACE inhibitors, diuretics, B-blockers**, ARBs and aldosterone blockers
DM with or without proteinuria	ACE inhibitors, ARBs or possibly B-blockers – all with a diuretic (Avoid dihydropyridine calcium antagonist alone) ***BP to < 130/80 most important***
Post-MI	B-blockers, ACE-inhibitors
Systolic hypertension (elderly)	Low dose ACE-inhibitor or ARB combined with a low dose diuretic (preferred). Alternative therapy: calcium channel blocker or B-blocker
Angina	B-blocker, calcium antagonist, ACE- inhibitor (not yet approved)
Pregnancy	Labetolol, methyldopa, calcium antagonists (ACEI contraindicated)
Prostatism	Alpha-blocker (not used alone)
Kidney insufficiency (non-diabetic)	ACE- inhibitor (ARB if ACEI not tolerated) *BP to < 120/80 most important*

*****Three or more medications often necessary to achieve BP goal
******Carvedilol is preferred for hypertension and has been shown to decrease proteinuria. Only two B-blockers are approved for HF (carvedilol and metoprolol XL/CR).

AF: On the basis of the AFFIRM and RACE trials for atrial fibrillation (AF), ***rate control can now be considered a primary approach to the treatment of AF, and rhythm control if used, can be abandoned early if it is not successful.***

It is no longer necessary to prescribe an anti-arrhythmic drug with a borderline benefit-risk ratio for an individual patient because of the belief that rate control therapy does the patient a greater disservice. This conclusion assumes patients are asymptomatic (70-75%) with the rate control strategy. A reasonable approach to the first episode of

AF is to do a careful assessment of symptoms and the underlying cardiac disease (history and physical examination and an echocardiogram). Rate control is a perfectly reasonable first option while completing the assessment to determine need for anticoagulation. As compared to rhythm control, rate control has advantages previously unappreciated.

In patients 65 and over, or those who have predisposing disease states, who are asymptomatic on rate control, nothing more is necessary other than careful attention to anticoagulation. In younger patients who don't convert, or those who remain symptomatic on rate control, cardioversion (initially without antiarrhythmic drugs, thereby avoiding potential side effects)—following anticoagulation guidelines—should be tried. If AF recurs and/or symptoms persist despite rate control, repeated cardioversion with the addition of antiarrhythmic drugs should be considered. Non-pharmacologic AV ablation with a permanent pacemaker is an option in patients who remain symptomatic despite adequate rate control or in those refractory to or intolerant to rhythm control. If a patient has an asymptomatic recurrence of persistent AF, rate control is certainly an option, especially if hypertensive. Pulmonary vein ablation, a relatively new modality is gaining more acceptance as a strategy for "cure" of younger patients with paroxysmal AF.

HF: ***The clinical trials for HF (systolic dysfunction) have shown us a stair-step incremental decrease in mortality with each additional drug or therapeutic intervention and, to get the best outcomes, we will have to use all of these treatments.*** This is a heavy burden for physicians—starting a medication or treatment which can have untoward effects—in an asymptomatic patient. The constant monitoring necessary to prevent or treat these complications is difficult. We don't seem to have as much difficulty when it's an interventional procedure which also has risk, but the burden of risk has been shifted.

The positive benefits of multiple drugs far outweigh the downside risk in HF, just as for primary and secondary prevention of CAD. In-hospital initiation of cardio-protective therapies has been demonstrated to markedly improve treatment utilization, long-term patient compliance and clinical outcomes in cardiovascular disease patients. Take advantage of that early window of opportunity. This is true post MI and for HF. After using diuretics to control volume, ACE inhibitors followed by beta-blockers digoxin and aldosterone blockers, should be added. ARBs should also be considered. Each one has been shown to have additional benefits on top of the previous therapies, just as the additional benefits of beta-blockers, ACE inhibitors and statins on top of ASA post MI.

Cardiac resynchronization therapy (biventricular pacing) for refractory HF, in those with BBB and implantable cardiac defibrillators, has been shown to reduce mortality and improve quality of life when used with other indicated medical therapy in those with systolic dysfunction.

hs-CRP: High sensitivity or cardiac CRP (*hs*-CRP) has been identified as a marker for inflammation associated with atherothrombosis. We agree with the AHA/CDC recommendation that it is reasonable to measure *hs*-CRP as an adjunct ("tiebreaker") to other major risk factors to further assess absolute risk for coronary heart disease (CHD) primary prevention.

This independent marker seems best used to detect enhanced risk where multiple risk factor scoring has projected a 10-year CHD risk in the range of 10-20% (Intermediate risk). This will justify more aggressive treatment in this group. An example of this would be a Metabolic Syndrome (MetS) patient who is calculated to have intermediate risk and has a high hs-CRP. We would treat that patient as high risk.

Cut points of risk for *hs*-CRP

Risk level	Hs-CRP *
Low	< 1
Average	1.0-3.0
High	> 3.0

*Levels of > 10mg/L should prompt the clinician to look for other signs of infection.

Exercise: ***"Survival of the fittest"…Patients with and without cardiovascular disease (CVD) who are less fit (less active) can improve their survival if they increase their level of fitness or physical activity (exercise a minimum of 30 minutes 5x/week, preferably daily).***

In terms of reducing mortality from any cause, improving exercise tolerance warrants as much clinical attention as decreasing other major risk factors for patients with, or at high-risk for, any CVD—CAD, HF etc. An added bonus is that hs-CRP is decreased with regular physical exercise.

MetS/T2DM: This is a problem that needs addressing both in our young population (more children are getting it) and our obviously higher risk older population. The December 8 issue of TIME magazine focuses on this problem, perhaps following our lead in last month's *Heartbeat.*

The "double whammy" of an aging population and the dangerous increase in inactivity and obesity in younger people threatens to bring about an epidemic of CVD greater than previously imagined. This epidemic is linked to a dramatic increase in the prevalence of type II diabetes mellitus (T2DM) which is often preceded by a cluster of metabolic abnormalities known as metabolic syndrome (MetS). Table 2 shows diagnostic criteria.

"Are you done with that?"

Table 2: Clinical ID of the Metabolic Syndrome*

Risk factor	Defining Level
Abdominal Obesity	Waist Circumference
Men	>40 in
Women	>35 in
Triglycerides (TG)	≥ 150mg/dL
HDL –C	
Men	<40mg/dL
Women	<50mg/dL
Blood pressure	≥130/≥85mmHg
Fasting glucose	≥ 110mg/dL

*Diagnosis is dependent on 3 or more factors

The task of heading off this growing epidemic is a comprehensive prevention program whose cornerstone is therapeutic lifestyle changes (TLC). Diet and exercise along with medical treatment of all abnormal parameters can prevent and or reverse this high-risk population from progressing to T2DM and the resultant CV complications. Agreement between patient and physician as to what their goals should be is the most important component of therapy. We have to be good coaches. Identification and treatment of the MetS is of enormous public health importance because it is associated with a marked elevation in CHD risk and affects nearly 25% of adults in the United States.

Clinical Management of MetS:

TLC

- Reduce weight—diet (enhances LDL-C lowering and reduces all risk factors)
- Exercise (reduces LDL-C and increases HDL-C and decreases hsCRP); beneficial for all risk factors

Treat lipid and non-lipid risk factors
(depending on 10yr CHD risk)

- Hypertension—(ACE-inhibitor/diuretic)
- Elevated TG—(fibrates)
- Low HDL-C—(niacin)
- Aspirin in CHD and those with > 6% 10yr CHD risk (decreases prothrombotic state)
- glucose > 110mg/dL (metformin or a glitazone)

Global Risk Reduction: Aggressive prevention of primary or recurrent events is the best treatment. In addition to treating the acute ischemic problem with revascularization, the underlying systemic disease process, a damaged vascular bed (atherothrombosis), must be treated. *"If prevention is your goal, don't focus on the hole, focus on the donut"—target the systemic disease not the lumen.* In patients with known CVD or equivalent disease or those at high-risk for it, we must treat atherothrombosis earlier. Combination therapy with statins, regardless of baseline levels, ASA, ACE inhibitors and beta-blockers, if no contraindication or intolerance, can result in a cumulative risk reduction of 70% and an absolute risk reduction of 13.1%.

HDL: The protective effects of HDL-C make raising low HDL-C an important part of our CVD global risk reduction strategy. Through reverse cholesterol transport, HDL "picks up the garbage," transferring cholesterol from vascular macrophages in peripheral cell membranes to the liver for biliary excretion, which decreases atherothrombosis. HDL-C is associated independently and inversely with CVD. Every 1% increase in HDL-C is associated with a 3% reduction of coronary events. ***A modest 5-10% increase in HDL-C can significantly reduce CHD event rates***. Niacin and/ or fibrates should be used as adjunctive treatment with statins and TLC if the HDL-C remains below 40mg/dL.

Blocking RAAS improves outcomes: Blocking the deleterious effects of the renin-angiotensin-aldosterone system by multiple different drugs has been shown to reduce mortality and morbidity in patients with CVD. It is no coincidence that the **use of *beta-blockers***, which are rennin inhibitors and block the conversion of angiotensinogen to angiotensin I, ***ACE inhibitors***, which block the conversion of angiotensin I to angiotensin II, ***ARBs*** which block the effects of angiotensin II at the receptor sites, and ***aldosterone blockers have all been associated with improved outcomes in large CV clinical trials*.** All four of these medications have also been shown to decrease proteinuria and slow renal disease progression. ACE inhibitors and ARBs have been shown to decrease the incidence of diabetes.

Many studies are now showing, as we suspected, that ARBs are a "safe and equally effective alternative strategy to ACE inhibitor therapy" for reducing the risks of death and cardiovascular events. However, *ACE inhibitors remain the logical first-line therapy for high risk patients* because of expense.

BNP for triage and assessing progress: Brain naturetic peptide (BNP), when used with clinical decision making and appropriate cutoffs, *allows us to make more accurate and early diagnosis of HF*. Low levels of BNP (< 100pg/ml) make the diagnosis of HF unlikely. A very high level (>500 pg/ml) strongly argues that the cause of dyspnea is HF. BNP testing reduced hospitalizations, the need for intensive care and total treatment time. Total treatment costs were reduced significantly by 25%.

Although the current rapid assay has only been approved for diagnosis, it may be of assistance in risk stratification, *determining the prognosis and severity of HF and also for monitoring response to treatment*. Finally, the role of BNP in the outpatient cardiology or primary care office may be critically important in referring patients for echocardiography, titration of therapies, and to assess the state of neurohumoral compensation of the patient.

Congratulations to our Physicians!! Your quality of outpatient care for primary and secondary prevention of CVD has definitely improved. Your more consistent usage of statins, ASA, ACE inhibitors and beta-blockers where appropriate (almost everyone) for CVD has made our job easier—and continues to result in improved outcomes for our patients. I believe your compliance to guidelines is above the reported averages. Your use of ACE inhibitors or ARBs in T1 and T2DM and in patients with azotemia is slowing renal disease progression. Per my personal interviews, compliance with guidelines on flu shot immunization has been fantastic. This, as you know, also decreases CVD morbidity and mortality. Great job!!

Happy Holidays!

On behalf of everyone @ SJHG

Mario, Jerry, Rich, Jay, Suren, Howard, John, Josh, Anil, Nader, Tim and Mitch

And the entire staff

We sincerely wish all of you a very Happy and Healthy Holiday season and a Happy New Year

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