Healthy Heart

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Honorary Editor :
Dr. Anish Chandarana

From the Desk of Hon. Editor:

Most physicians believe that tachycardia at rest is prognostically undesirable, but importance of resting heart rate (HR) as a prognostic factor and as a potential therapeutic target is not yet generally well accepted. The findings of recent large epidemiologic studies have reemphasized that resting HR is an independent predictor of cardiovascular and all-cause mortality in men and women with and without established cardiovascular disease. Many clinical trials also have suggested that HR reduction is an important mechanism of benefit of beta-blockers (BB) and other heart-rate lowering drugs used after acute myocardial infarction, in chronic heart failure, and in stable angina pectoris. Studies have revealed that high HR has a deleterious effect on occurrence of atherosclerosis, myocardial ischemia, ventricular dysfunction and arrhythmias. Though it is difficult to define an optimal HR for a given individual, keeping the fact that studies have found a continuous increase in risk with HR above 60/min, it seems appropriate to maintain resting HR as close as possible to this.

- Dr. Anish Chandarana

Heart Rate in Clinical Practice

HR assessment is a critical part of patient examination. HR has been reported to decrease with age, and is higher in women than in men. HR shows a circadian rhythm, being substantially higher during waking hours and it also changes with posture, few beats/min higher in the sitting position compared with the supine position. Over the last many years we, as physicians, have understood and perceived that tachycardia at rest is prognostically undesirable. But importance of resting HR as a prognostic factor and as a potential therapeutic target is not yet well accepted. In the present chapter we will learn about epidemiological evidences linking HR to various events, potential mechanisms by which this happens and data on effects of therapeutic interventions aimed at reducing HR on cardiovascular morbidity and mortality in different patient populations. Change in HR which happens acutely because of some infectious or inflammatory disease or during/immediately after exercise is also important, but that has not been discussed in this chapter. Similarly we have not discussed the data on association of HR reduction achieved by regular practice of exercise/yoga and clinical benefits.

Epidemiological Data Linking HR and Clinical Events

A stream of alternative medicine believes that we are all born with a certain number of heart beats. In many mammals it has been observed that life expectancy is in inverse proportion to their resting HR. A significant association between resting HR and cardiovascular as well as all-cause mortality has been reported in many epidemiologic studies over the last 20-30 years, in both the general population and in those with cardiovascular diseases, including hypertension (HT),acute myocardial infarction (AMI), and heart failure (HF) or left ventricular (LV) dysfunction. The Framingham study did show increased risk of all cause mortality with increased resting HR and this association was stronger with advanced age. One study done by Jouven X et al on 5,713 working men, age 42 to 53 years and without known or suspected

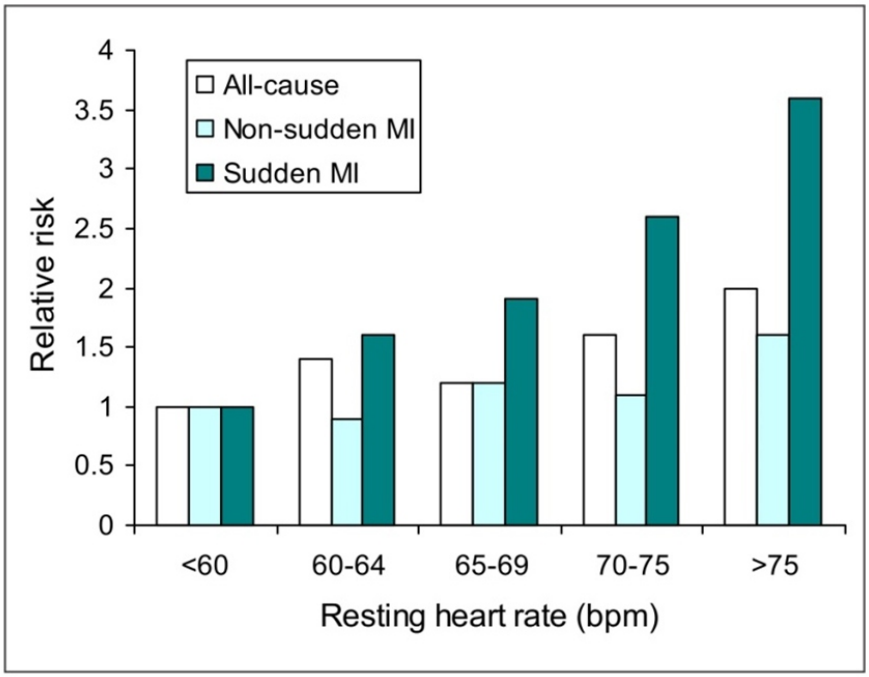

Fig 1. Heart Rate and Mortality in Healthy Men : Relative risk of death from any cause, nonsudden death from MI, and sudden death from MI by quintiles of resting heart rate in 5,713 men without known or suspected heart disease Jouven et all. bpm = beats/min. Resting Heart Rate in Cardiovascular Disease, Kim Fox et al, J Am CollCardiol. 2007;50(9):823-830. doi:10.1016/j.jacc.2007.04.079

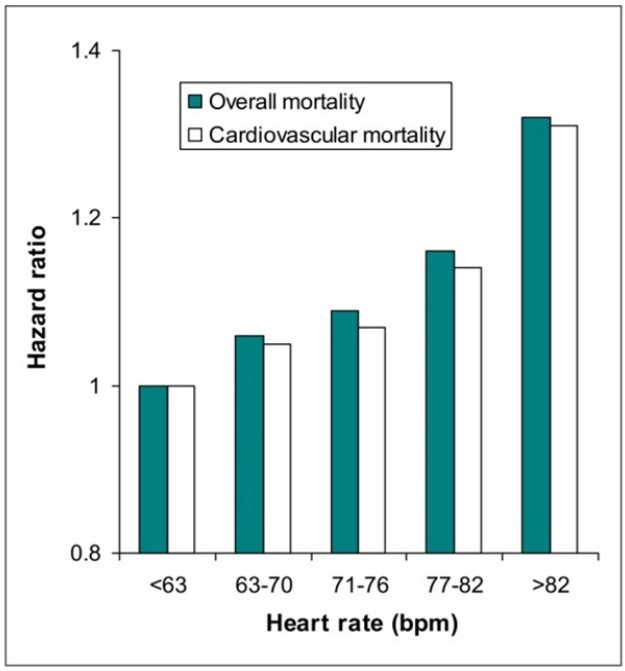

Fig. 2 Heart Rate and Mortality in Coronary Artery Disease : Relationship between hazard ratio and resting heart rate for all-cause and cardiovascular mortality in 24,913 patients with suspected or proven coronary artery disease. Based on data from Diaz et al. (5).bpm = beats/min. Resting Heart Rate in Cardiovascular Disease, Kim Fox et al, J Am CollCardiol. 2007;50(9):823-830. doi:10.1016/j.jacc.2007.04.079

cardiovascular disease, who then were followed up for a mean of 23 years showed all-cause mortality and sudden and nonsudden death from AMI, each increased progressively with resting HR, and remained significant after adjustment for exercise capacity (evaluated by bicycle ergometry), age, body mass index, level of physical activity, diabetes, systolic arterial pressure and other factors. The relationship was steepest for sudden death (Fig. 1). Another such study by Diaz A et al involved 24,913 men and women with suspected or proven coronary artery disease who participated in the Coronary Artery Surgery Study registry. At the median follow-up of 14.7 years, all-cause and cardiovascular mortality was directly related to resting HR at study entry. This was independent of concomitant hypertension, diabetes, habit of smoking, LV ejection fraction and number of diseased coronary vessels. Hazards ratios were similar for men and women, old (>65 years) and young patients, hypertensive and normotensive patients, diabetic and nondiabetic patients, those with LV ejection fraction >50% and<50%, and those with a BMI>27 and<27 kg/m2(Fig.2).Palatini P et al suggested that positive association between high HR and all cause and/or cardiovascular mortality was independent of other risk factors for atherosclerosis or cardiovascular events at all ages and has a consistency similar to that of smoking. Resting HR currently is included in risk assessment indices for patients after acute coronary syndromes (e.g., GRACE risk prediction score and the TIMI risk score).

How Does Heart Rate Affect Cardiovascular Pathophysiology?

In animals and humans, HR is directly associated with progression of coronary atherosclerosis and also has been significantly related to the likelihood of disruption of pre-existing atherosclerotic

plaque. HR is strongly and directly associated with arterial rigidity in hypertensive patients, after adjustment for age and blood pressure. The basis of myocardial ischemia is impaired balance between myocardial oxygen demand and supply. Heart rate influences both factors, as higher HR increases work load of the heart and by shortening the diastolic phase it reduces coronary perfusion time. The likelihood of developing ischemia is related to the baseline HR and the magnitude and duration of the increase. HR also influences whether ischemic episodes trigger serious arrhythmias. Abrupt-onset myocardial ischemia is more likely to result in ventricular tachycardia and fibrillation with a high HR than in those with a lower HR.

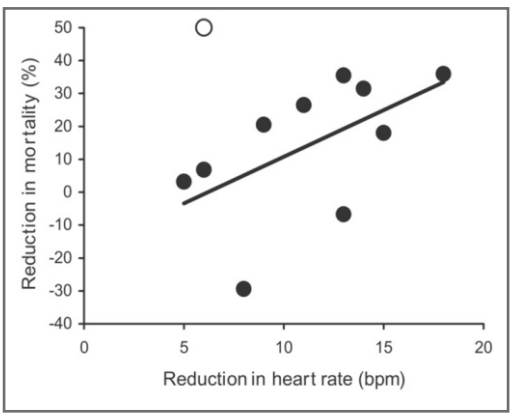

Fig. 3 HR Reduction and Mortality After MI : Relationship between the mean reduction in heart rate and the mean change in mortality (relative to placebo) in different randomized, placebo-controlled trials of beta-blockers after MI. The linear regression line ($r = 0.6$, $p < 0.05$) was fitted excluding the smallest study (open circles). Modified and based on data from Kjekshus (17). bpm = beats/min. Resting Heart Rate in Cardiovascular Disease, Kim Fox et al, J Am CollCardiol. 2007;50(9):823-830. doi:10.1016/j.jacc.2007.04.079

Benefits of Heart Rate Reduction: Evidences and Mechanisms

Variety of medicines like beta-blockers (BB), nondihydropyridine calcium channel blockers (CCB), ivabradin, digitalis and few other anti-arrhythmic medicines have shown HR reducing effects in normal people or patients with various cardiovascular diseases.

Chronic Stable Coronary Artery Disease: Many trials done with BB, CCB and newer drug ivabradin have shown reduced episodes of ischemia and angina due to lowered resting as well as exercise HR achieved by these drugs.

Acute Myocardial Infarction: Many trials have shown that the beneficial effects of BB after AMI are related to reduction in HR. Kjekshus reviewed early randomized trials which used BB within 6 h of the onset of symptoms. Meta analysis of six trials (N = 1427) which estimated infarct size and HR correlation, showed that mean reduction in infarct size was directly related to the mean reduction in HR ($p<0.001$). Similarly in 11 placebo-controlled long-term trials of BB (N=16,000) after AMI, a significant association was found between the reduction in HR and reduction in mortality (Fig.3).

Heart Failure: Kjekshus and Gullestad showed not only a relationship between reduction in HR and mortality in treated patients of heart failure, but also showed that agents which increased HR tended

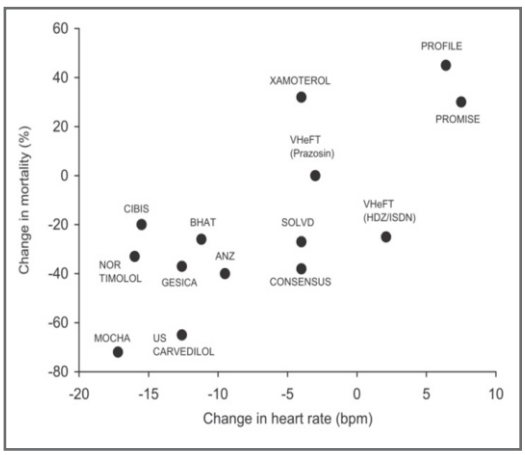

Fig. 4 HR Reduction and Mortality in HF: Relationship between mean change in heart rate and mean change in mortality in studies of patients with chronic HF. (Kjekshus and Gullestad). ANZ = Australia/New Zealand Heart Failure Research Collaborative Group; BHAT = Beta Blocker Heart Attack Trial; bpm = beats/min; CIBIS = Cardiac Insufficiency Bisoprolol Study; CONSENSUS = Cooperative North Scandinavian Enalapril Survival Study; GEISCA = Grupo de Estudio de la Sobrevida en la InsuficienciaCardiaca en Argentina; HDZ/ISDN = hydralazine/isosorbidedinitrate; MOCHA = Multicenter Oral Carvedilol Heart Failure Assessment; NOR TIMOLOL = Norwegian Multicentre Study Group; PROFILE = Prospective Randomized Flosequinan Longevity Evaluation; PROMISE = Protection Devices in PCI-Treatment of Myocardial Infarction for Salvage of Endangered Myocardium Study; SOLVD = Studies of Left Ventricular Dysfunction; US CARVEDILOL = U.S. Carvedilol Heart Failure Study Group; VHeFT = Vasodilator in Heart Failure Trials; XAMOTEROL = Xamoterol in Severe Heart Failure Study Group.Resting Heart Rate in Cardiovascular Disease, Kim Fox et al, J Am CollCardiol. 2007;50(9):823-830. doi:10.1016/j.jacc.2007.04.079

to increase mortality(Fig.4). In CIBIS (Cardiac Insufficiency Bisoprolol Study)II trial, baseline HR and HR change both were significant predictors of mortality. The best prognosis was seen in patients with the lowest baseline HR and with the highest HR reduction. Analysis of data from the COMET (Carvedilol or Metoprolol European Trial) study showed that HR achieved during BB treatment was a significant independent predictor of mortality, but it could not explain greater survival benefit with carvedilol compared with metoprolol. In the MERIT-HF (Metoprolol CR/XL Randomized Intervention Trial in Congestive Heart Failure) study, the benefits with metoprolol were independent of the change in HR achieved, suggesting that HR reduction is not the only mechanism of benefit of BB in heart failure. SHIFT (Systolic Heart failure treatment with the If inhibitor ivabradin Trial) study showed reduced composite endpoints of deaths and HF admissions when ivabradin was added to preexisting BB therapy in patients with stable HF who had LVEF</=35% and HR was =/>70 beats/minute. This did prove that it is the magnitude of HR reduction that improves outcomes in stable HF patients.

Hypertension: In a meta-analysis of more than 60,000 patients in 9 large beta-blocker trials, use of BB (mainly atenolol) in patients with HT has been shown to have a greater risk of cardiovascular events (all-cause mortality, cardiovascular mortality, myocardial infarction, stroke, and heart failure, all p<0.0001) with a lower heart rate. Pulse wave dysynchrony occurring due to lowered HR by atenolol leads to elevated central aortic pressure, and that in turn, has a deleterious effect on LV-aortic coupling, LV afterload, LV hypertrophy, and, ultimately, the risk of cardiovascular events. The hypertension paradox observed with BB (mainly atenolol) cannot be solely explained by pharmacologic HR slowing, and findings should not be extrapolated to pharmacologic interventions aiming at pure heart rate reduction.

Atrial Fibrillation: Improved survival through reduction of HR by BB is shown in atrial fibrillation patients who have history of MI or heart failure. In large rate versus rhythm control trials in patients with atrial fibrillation, HR reduction tended toward improved survival when compared with a rhythm control strategy. But there is no evidence showing that strict HR control was superior to less stringent rate control. Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT AF) showed, in patients with permanent AF, there is a J-shaped relationship between heart rate and mortality. These findings support the hypothesis that lenient rate control in permanent AF may not be optimal.

Sinus Node Disease: Low HR seen in patients with this conduction system disease is not associated with better cardiovascular outcomes.

Conclusion:

HR is a risk factor for cardiovascular mortality, independent of other accepted risk factors, demographic and physiological characteristics in people without and with diagnosed cardiovascular disease. HR reduction achieved by BB in patients with post MI status, stable heart failure and chronic stable heart disease has been shown to affect cardiovascular events favorably. But the same intervention has not been shown to have similar impact in hypertensive or normal individuals. It is worth noting that BB, CCB, and physical conditioning have multiple additional actions other than HR lowering. It is difficult to define an optimal HR for a given individual, keeping the fact that studies have found a continuous increase in risk with HR above 60/min, it seems appropriate to maintain resting HR as close as possible to this.

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CIMS Learning Center

Advanced ECG Learning-Certification Course

Course Directors : Dr. Ajay Naik / Dr. Vineet Sankhla / Dr. Vipul Kapoor
Date : February 28, 2016 (Sunday)
Duration : Half day
Number of seats : 50
Venue : CIMS Auditorium

Program Overview:

Advanced ECG course is designed for practicing physicians having basic knowledge of ECG. This program covers a wide range of ECG lectures and tips to identify various type of simple & complex arrhythmias and rare ECG abnormalities.
The aim of this course is to present complex various ECG diagnosis pattern in a simple and easy to understand manner.

Program Highlights:

- Supraventricular arrhythmias: diagnosis & mangement
- Ventricular arrhythmias: diagnosis & mangement
- Pharmacotherapy in arrhythmia mangement
- Evaluation of syncope
- EP study and RF ablation
- Disorders of sinus node and atrioventricular conduction
- Device therapy (Pacemakers / ICD / CRT)
- Atrial fibrillation: rhythm and rate control (Pharmacologic & Non-Pharmacologic)

Registration Fees	: ₹ 1,000/- (Up to one month before course date)
Registration Fees	: ₹ 1,500/- (Within 15 days before course date)
Spot Registration Fees	: ₹ 2,000/-

Visit
www.cims.me/clc
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› Certificate of attendance will be given at the end of the course

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CIMS Learning Center

Clinical Cardiology and Critical Care Refresher Week-Certification Course

Course Directors : Dr. Bhagyesh Shah, Dr. Vipul Thakkar, Dr. Vipul Kapoor, Dr. Tejas V. Patel, Dr. Milan Chag
Date : February 29 to March 5, 2016
Duration : 1 Week (Monday to Saturday)
Number of seats : 5 (Very Limited)-Highly Interactive

FIRST TIME IN INDIA

Program Overview: This program is intended to refresh and enhance the ability of candidates for early recognition, management of common cardiovascular and critically sick patients. They will be exposed to various diagnostic procedures related to cardiology including ECG, Echocardiography, Dobutamine Stress Echo, Holter Monitoring, and Cardiac Radiology. Delegates would have opportunity to see how cardiologist evaluate patient in their daily OPDs and would also be shown Angiography and Angioplasty procedure of these patients. They will be taken to ICU, CCU and Intensive Unit during their rounds. They will also have opportunity to handle critically sick patient in emergency department. Refresher lectures will be delivered related to pharmocology, pathophysiology, guidelines and important medical disorder related to cardiology and critical care medicine.

(A) Registration Fees without Hotel Accomodation

Registration Fees	: ₹ 25,000/-**
Registration Fees	: ₹ 30,000/-***
Spot Registration Fees	: ₹ 35,000/-

(B) Registration Fees with Hotel Accomodation

1. 3 Star Hotel Accomodation	: ₹ 40,000/- **
2. 4 Star Hotel Accomodation	: ₹ 50,000/-***
3. Spot Registration Fees	: ₹ 55,000/-

** (Up to one month before course date) *** (Within 15 days before course date)

› Certificate of attendance will be given at the end of the course

Management of Drug Resistant Tuberculosis-Certificate Course

Course Directors : Dr. Surbhi Madan / Dr. Bhavini Shah
Date : April 10, 2016 (Sunday) **Venue :** CIMS Auditorium

Program Overview: :
This course is designed for physicians who are involved in the management of patients with tuberculosis. Due to emergence of drug resistant tuberculosis, the approach towards treatment has changed and is continuously evolving. It is important to have updated knowledge about the new diagnostic strategies and treatment approaches for optimal management. The aim of this course is to discuss the same with the help of clinical cases.

Program Highlights:
- Newer diagnostics: Emphasis on molecular tests
- Importance of culture and DST (Drug susceptibility testing)
- Define various categories of drug resistant TB
- Treatment of drug resistant TB- Program based or individualized?
- Important adverse effects of second line drugs
- Immune reconstitution in tuberculosis: Clinical relevance
- Role of surgery in treatment
- Newer drugs
- Interactions amongst antituberculous drugs

Registration Fees	: ₹ 1,000/- (Up to one month before course date)
Registration Fees	: ₹ 1,500/- (Within 15 days before course date)
Spot Registration Fees	: ₹ 2,000/-

› Certificate of attendance will be given at the end of the course

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