

## **HRT risk on cardiovascular events**

### **1. What is the risk of hormone replacement therapy (HRT) increasing cardiovascular events? I see that HRT reduces C-reactive protein, so, is it helpful in preventing cardiovascular events?**

Question submitted by Dr. T. Subramanian, Hamilton, Ontario

The study that has the most influence on our current approach to the management of the post-menopausal patient is the Women's Health Initiative (WHI) Study.

This was a randomized primary prevention study involving over 16,000 women. The arm of the study comparing the combination of estrogen/progesterone with placebo was terminated early, showing at that point appreciable risk of vascular end-points, which included coronary events and strokes (this risk increased respectively by seven and by eight per 10,000 women who were treated for one year).

C-reactive protein levels should be considered as one marker among many and while helpful in the risk stratification of patients, it should not—at this point—take away from the results of the WHI study without robust new data suggesting otherwise.

Answered by:

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## ***β-blockers post-MI***

### ***2. How should a cardiologist interpret and alter practices, if at all, after the recent controversy surrounding post-MI atenolol?***

Question submitted by Dr. Neil Skjodt, Edmonton, Alberta

The Clopidogrel and Metoprolol in Myocardial Infarction Trial (COMMIT), randomized 45,852 patients with ST-elevation MIs (STEMIs) within 24 hours of symptom onset to metoprolol or placebo.<sup>1</sup> At enrollment, three doses of 5 mg of metoprolol were given intravenously (IV) every two minutes to three minutes, unless heart rate was < 50 bpm, or the patient's systolic BP was < 90 mmHg. Subsequent administration of oral metoprolol, (50 mg, q.i.d.) for the first day, with 200 mg controlled-release thereafter, occurred unless strong contraindications existed.

Randomization to metoprolol had no benefit on the death rate (in-hospital death was 7.7% with metoprolol vs. 7.8% with placebo). There was less reinfarction (2% with metoprolol vs. 2.5% with placebo,  $p < 0.001$ ) and less ventricular fibrillation (2.5% with metoprolol vs. 3% with placebo,  $p = 0.001$ ), which was balanced by increased cardiogenic shock (5% with metoprolol vs. 3.9% with placebo,  $p < 0.00001$ ).

This megatrial demonstrates that the early, aggressive use of β-blockers in all STEMI patients was *not* beneficial.

Judicious use of both IV and oral β-blockers in appropriate STEMI patients remains prudent. The patients that most likely benefit from the IV administration of β-blockers are those with tachycardia and hypertension, especially in the face of ongoing ischemic chest pain. Decreased myocardial oxygen demand, though lowering BP and heart rate, will limit infarct size in conjunction with timely reperfusion.

At the other end of the spectrum, patients with bradycardia and/or hypotension may well be exposed to increased risk with aggressive IV β-blocker usage, so it is discouraged. Special consideration should be given to patients with tachycardia in the face of normal or low-normal BP, since the tachycardia may be a compensatory mechanism for impending heart failure and shock.

The current approach of most practicing physicians is the initiation of oral β-blocker therapy, at a low dose, in the early stages of a MI, with subsequent titration to achieve appropriate heart rate and BP target.

#### Reference

1. Chen ZM, Pan HC, Chen YP, et al: Early intravenous then oral metoprolol in 45,852 patients with acute myocardial infarction: Randomised placebo-controlled trial. *Lancet* 2005; 366 (9497):1622-32.

Answered by:

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## Treating PAT

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### 3. What is the treatment of PAT for an asthmatic patient with two to three episodes per week, lasting 15 minutes to 20 minutes each and with no symptoms other than vague discomfort and anxiety?

Question submitted by Dr. Michel Dubé, L'Epiphanie, Québec

Paroxysmal atrial tachycardia (PAT) is often triggered by catecholamines. In an asthmatic, PAT may be triggered by B-agonist inhalers. The first treatment for PAT in an asthmatic would therefore be to minimize the use of sympathomimetics as much as possible. In addition, establishing symptom-rhythm correlation with either an external loop monitor or a Holter monitor is essential.

The decision to proceed with medical therapy is based either on symptoms or on the presence of fast atrial tachycardia that lasts for prolonged periods of time, which may result in tachycardia-induced cardiomyopathy. If your patient is only having 20 minute episodes and does not find

the symptoms intolerable, then no therapy is a reasonable option. If the arrhythmia persists and is symptomatic, the next line of therapy would be a cardiac specific calcium channel blockade with diltiazem. If that is unsuccessful, then trials of the Class 1C agents, such as flecainide, would be indicated.

Before using flecainide, it is important to document that there is no coronary artery disease (CAD), since these drugs are contraindicated in patients with CAD. Depending on the rate of the atrial tachycardia, Class 1C agents should be used in conjunction with an AV nodal blocking agent to prevent slowing of fast atrial tachycardias with 1:1

conduction to the ventricle. For persistent and symptomatic atrial tachycardias, curative radiofrequency ablation by an electrophysiologist has a success rate of 80% to 90%.

Answered by:

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## CCBs as secondary prevention

### 4. Should calcium channel blockers (CCBs) be used as secondary prevention for CAD if $\beta$ -blockers are contraindicated (i.e., asthma)?

Question submitted by Dr. Graham E. White, Parksville, British Columbia

$\beta$ -blockers are widely used and effective in patients with coronary artery disease (CAD) and symptomatic angina. They are also indicated in patients with a recent MI. Their use in asymptomatic CAD—to prevent future events—is less well established.

As with most medications, there are conditions where some drugs should be used with caution. True asthma is one where  $\beta$ -blockers—especially those that are non-selective and also block  $\beta$ -2 receptors—can precipitate an acute asthma exacerbation. Even cardioselective  $\beta$ -blockers should be used with caution if asthma

is severe and the patient should have a  $\beta$ -2 agonist bronchodilator easily available to them. Long-acting calcium antagonists can be considered as alternatives to a  $\beta$ -blocker in patients with asthma and they are effective for angina and BP control; but, are less well proven for secondary prevention and are best avoided if the patient also has symptomatic systolic heart failure. 

Answered by:

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*Long-acting calcium antagonists can be considered as alternatives to a  $\beta$ -blocker in patients with asthma; but they are less well proven for secondary prevention and are best avoided if the patient also has symptomatic systolic heart failure.*

