

Non-Lipid Benefits

1. What are the emerging non-lipid benefits of statin therapy?

Question submitted by: Dr. Steven Kravcik, Crescent, Ontario

There is no doubt that statins have beneficial effects on CV mortality and morbidity, primarily through their lipid-lowering effects. They also appear to have a number of potentially beneficial effects independent of their lipid lowering effects. Most of these effects seem to be related to their direct effects on the endothelium. Endothelial dysfunction is a critical component of organ injury after acute ischemic events and in the chronic disease states such as diabetes and dyslipidemia. Laboratory studies suggest that these effects are primarily related to enhancing the bioavailability of nitric oxide in the vascular endothelium. The main effects of statins on the endothelium include:

- Improved endothelial function through increased nitric oxide production

- Anti-inflammatory effects by reducing acute phase proteins including C-reactive protein (hs-CRP), inflammatory cytokines, and cellular adhesion molecules
- Antioxidant effects by scavenging superoxide ions and superoxide generators such as isoprenoids
- Antithrombotic effects by shifting the fibrinolytic balance towards fibrinolysis and reducing platelet aggregation
- Stabilizing atherosclerotic plaques
- Antiproliferative effects inhibiting smooth muscle cell proliferation

The next important question is whether or not these laboratory findings translate into clinical benefit. Studies in the small groups of patients or in sub-groups of larger clinical trials

have been encouraging. Larger prospective randomized clinical trials are necessary to establish their clinical effects and importance.

Answered by:
Dr. Wayne Warnica

Following Hemoglobin in Congestive Heart Failure

2. Should hemoglobin be followed? Is there a trade-off in congestive heart failure (HF)?

Question submitted by: Dr. Patricia Menard, Antigonish, Nova Scotia

Anemia is common in HF patients and portends a poor prognosis. A recent study demonstrated that for each 1 g/dl decrease in hemoglobin, there was a 20% increase in the multivariate adjusted risk of death. What is uncertain is whether anemia is a marker or is a mediator of the adverse prognosis.

The prevalence of anemia is higher with advanced New York Heart Association functional class, older age, worse renal function and more comorbidities.

Cardiologists have only lately started to recognize, evaluate and treat anemia. Tang, *et al* found that < 20% of all anemic HF patients had a laboratory evaluation for the anemia and

only 30% had a repeat hemoglobin within six months.

We do not know whether treatment for anemia with IV iron or erythropoiesis-stimulating proteins (ESPs) reduces the risk associated with anemia. IV iron therapy is being studied in a large randomized trial, Iron Supplementation in Heart Failure Patients With Anemia (IRON-HF). Phase 2 clinical trials of anemia in HF patients (n=475 patients) have shown that ESPs can increase hemoglobin, improve HF symptoms and improve exercise capacity and may reduce morbidity/mortality (hazard ratio 0.67, 95% confidence interval 0.44 to 1.03, p=0.07). This hypothesis is being tested in an ongoing trial, the Reduction in Events with darbepoetin alpha in Heart

Failure trial (RED-HF), a double-blind randomized trial in 3,400 anemic New York Heart Association functional class II to IV systolic HF patients.

If anemia persists, evaluation and treatment of the underlying cause is appropriate.

Resources

1. Tang WH, Tong W, Jain A, et al: Evaluation and Long-Term Prognosis of New-Onset, Transient and Persistent Anemia In Ambulatory Patients With Chronic Heart Failure. *J Am Coll Cardiol* 2008; 51(5):569-76.
2. Levy WC: Anemia in Heart Failure: Marker or Mediator of Adverse Prognosis? *J Am Coll Cardiol* 2008; 51(5):577-8.

Answered by:
Dr. J. G. Fodor



Cardiac Pathology in Refeeding Syndrome

3. Can you please tell me more about cardiac pathology in the refeeding syndrome?

Question submitted by: Dr. Lorne Pilot, Saskatoon, Saskatchewan

Refeeding syndrome describes a constellation of abnormalities that occur as a result of reinstitution of nutrition to patients who are starved or severely malnourished. The syndrome was first described in Far East war prisoners after the Second World War.

During starvation, heart rate, BP and left ventricular mass decrease significantly. The ECG may demonstrate decreased voltages and a prolonged QT interval.

With refeeding, patients can develop fluid and electrolyte disorders, especially hypokalemia and hypophosphatemia. Heart failure, arrhythmias and sudden death are the most common cardiac complications.

The most important steps are to identify patients at risk for developing refeeding syndrome, institute nutrition support cautiously, and correct and supplement electrolyte and vitamin deficiencies.

Resources

1. Crook MA, Hally V, Panteli JV: The Importance of the Refeeding Syndrome. *Nutrition* 2001; 17(7-8):632-7.
2. Kraft MD, Btaiche IF, Sacks GS: Review of the Refeeding Syndrome. *Nutr Clin Pract* 2005; 20(6):625-33.

Answered by:
Dr. Brett Heilbron

Referring an AF Patient for Cardiac Ablation

4. What would be the optimal time to refer a patient with a diagnosis of atrial fibrillation (AF) for cardiac ablation?

Question submitted by: Dr. S. Gynspon, Toronto, Ontario

Recent studies have indicated that many patients with AF, particularly if they are minimally symptomatic, tolerate their cardiac medications well, have a long duration of persistent AF and/or have significant underlying structural cardiac disease, may be best managed with a strategy of rate control and anticoagulation rather than a strategy of rhythm control.

In those patients best suited to a strategy of rhythm control (usually younger, more symptomatic, poorly tolerant of antiarrhythmic medications and minimal structural cardiac disease), a catheter ablation procedure may be an attractive option.

The advantages of catheter ablation are:


- Improvement in AF-related symptoms

- Reduction or discontinuation of antiarrhythmic medications (with their attendant risks and side-effects)

The disadvantages are:

- Major complication rate of up to 6% from the procedure itself (including pulmonary vein stenosis, thromboembolism, atriopharyngeal fistula, cardiac tamponade)
- High one-year failure rate, up to 40% depending on patient selection and operator skill
- Ongoing need for anticoagulation with warfarin in most patients
- Long waiting times for the procedure in Canada, owing to the shortage of Electrophysiologists and Electrophysiology lab time

Many Electrophysiologists prefer to attempt an ablation procedure

only after a “good” patient has tried and failed at least two antiarrhythmic drugs and remains very symptomatic from AF. 

Resource

1. European Heart Rhythm Association, Heart Rhythm Society, Fuster V, et al: ACC/AHA/ESC 2006 Guidelines for the Management of Patients With Atrial Fibrillation. A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Revise the 2001 Guidelines for the Management of Patients With Atrial Fibrillation). J Am Coll Cardiol 2006; 48(4):149-246.

Answered by:
Dr. Brett Heilbron