of the study. Taking into account these determinants of infarct size in the experimental design of future trials will help to improve their accuracy and power to explore future treatments that aim to prevent lethal reperfusion injury.

At a time of major difficulties in supporting the cost of our health-care systems, Bøtker and colleagues have shown that a non-invasive, simple, safe, and cheap intervention, possibly done by a paramedic before hospital admission, can significantly increase myocardial salvage; they have also shown the benefit of an integrated prehospital and inhospital therapeutic strategy. Following the lessons of experimental models, Bøtker and colleagues were able to show that remote conditioning can significantly increase myocardial salvage in patients with STEMI, which suggests that the technique might represent a new powerful treatment option for such patients. Their study confirms proof-of-concept clinical studies and suggests that lethal reperfusion injury is the next major target for the treatment of patients with acute myocardial infarction. Any enthusiasm arising from this encouraging study must, however, be tempered by the need to show actual clinical benefit in larger-scale clinical studies.

"Michel Ovize, Eric Bonnefoy
Hospices Civils de Lyon, Hôpital Cardio-vasculaire et Pneumologique and University Lyon 1, Lyon, France (MO, EB); and Hospices Civils de Lyon, Hôpital Cardio-vasculaire et Pneumologique and INSERM 886, 69008 Lyon, France (MO)
michel.ovize@chu-lyon.fr

We declare that we have no conflicts of interest.


Balancing the benefits of statins versus a new risk—diabetes

All drugs have side-effects. Indeed, all interventions (including even exercise programmes) have side-effects. The balance in medicine is to evaluate the benefits and weigh them against the risks. For statins, the benefits in reducing clinical events have been shown in a multitude of trials with more than 500 000 patient-years of treatment. This benefit has led to their inclusion in national guidelines as a key component of both primary and secondary prevention. The side-effects most often discussed with statins are increases in liver-function tests, muscle aches, and, more rarely, rhabdomyolysis.

Most recently, development of diabetes was suggested in a large randomised trial of rosuvastatin for primary prevention. Many questions arose: was this a true finding or the play of chance; and, if real, was the finding particular to this statin or a class effect? Then, additional questions we would ask are: is the effect a large or small one? And how does this risk balance against the known benefits of statins? Has this effect been seen with other drugs? Finally, what are the practical clinical implications—ie, what do I need to do for my patients?

In The Lancet today, Naveed Sattar and colleagues present a collaborative meta-analysis of randomised trials with statins in which they address many of these issues by collecting data from 13 large placebo-controlled trials. These meta-analysts found that there was a consistent finding of a higher risk of developing diabetes. Over a mean of 4 years in just over 91 000 individuals, 2226 assigned statins and 2052 assigned control treatment developed diabetes. There was a 9% increase in risk (odds ratio 1.09; 95% CI 1.02–1.17)—ie, a small increased risk. The risk seemed to be present mostly in older patients, with no risk seen in younger patients (age ≤60 years). They found little statistical heterogeneity between trials and statins. Thus this finding does seem to be a class effect of statins.

This effect seems almost paradoxical—how could a statin increase the risk of developing diabetes
when statins are known to have such a benefit in reducing cardiovascular events in patients with known diabetes.\(^9\) However, several other cardiovascular drugs have also been associated with an increase in the risk of developing diabetes.\(^8\) Thiazide diuretics (notably hydrochlorothiazide and chlorothalidone) have this same association.\(^7\) β blockers are also known to lead to a higher risk of developing diabetes.\(^6\) Among lipid-modifying agents, niacin is known to have an adverse metabolic effect with a higher risk of developing diabetes.\(^5\) Thus several other classes of cardiovascular drugs also have been reported to have an association with an increased risk of developing diabetes.

Hence we have a very beneficial class of drugs with an adverse risk—so one needs to balance what this risk would be in absolute terms and how it stacks up against the benefit. Sattar and colleagues calculated, with data from the Cholesterol Treatment Trialists’ Collaborators,\(^2\) that the absolute risk of developing diabetes was one case per 1000 patient-years of treatment. They put this another way: if you treat 255 (95% CI 150–852) patients for 4 years with a statin, one additional patient would develop diabetes than if they had not been treated with a statin. Still with data from the Cholesterol Treatment Trialists’ Collaborators,\(^2\) they estimated that 5·4 deaths or myocardial infarctions would be avoided over those 4 years, and nearly the same number of strokes or coronary revascularisation procedures would also be avoided. Therefore the benefit in preventing total vascular events to the risk of diabetes is a ratio of about 9:1 in favour of the cardiovascular benefit—the benefit seems to greatly outweigh the risk.

Nonetheless, this newly identified risk does warrant monitoring, and, as such, in addition to periodic monitoring of liver-function tests and creatine kinase, it seems reasonable to add glucose to the list of tests to monitor in older patients who are on statins. Thus, whilst a new risk of statins has been identified, the risk seems small and far outweighed by the benefits of this life-saving class of drugs.

Christopher P Cannon
Cardiovascular Division, Brigham and Women’s Hospital and Harvard Medical School, Boston, MA, USA; and TIMI Study Office, Boston, MA 02115, USA
cpcannon@partners.org

I am a senior investigator on the TIMI Study Group. Within the past 2 years, I have received research support from Accumetrics, AstraZeneca, Bristol-Myers Squibb/Sanofi Partnership, GlaxoSmithKline, Intekrin, Merck, Novartis, and Takeda. I serve as a clinical adviser to and hold equity in Automedics Medical Systems.