Challenges for the Basis of Practice

Statins in the Treatment of Heart Failure

Pim van der Harst, MD; Rudolf A. de Boer, MD

The 3-hydroxy-3-methylglutaryl coenzyme-A inhibitors or statins have been shown to reduce morbidity and mortality in patients with coronary artery disease or those at increased risk of coronary artery disease (Table). Consequently, statin therapy has become the cornerstone treatment in primary and secondary prevention of coronary artery disease for almost every patient category. However, the case for the use of statin therapy in the most advanced stage of the cardiovascular disease continuum, namely patients with chronic heart failure (CHF) has been disputed. Until recently, we simply lacked data because patients with CHF had been systematically excluded from large clinical statin trials (Table). Although a few smaller, uncontrolled trials suggested that statins may be beneficial in CHF too, there is some reason to think that statins may rather have harmful effects in patients with CHF. Recently, the long-awaited CORONA [Controlled Rosuvastatin Multinational Trial in Heart Failure] and the GISSI-HF [Gruppo Italiano per lo Studio della Sopravvivenza nell’Infarto Miocardico Heart Failure] trials were completed. These trials prospectively investigated

Table. Clinical Outcome in Large (N>2500), Placebo-Controlled Statin Trials and Patients With CHF in These Trials

<table>
<thead>
<tr>
<th>Trial Acronym/Treatment, Year</th>
<th>No. of Patients</th>
<th>Intervention*</th>
<th>Prevention</th>
<th>Conclusion</th>
<th>Patients With CHF</th>
</tr>
</thead>
<tbody>
<tr>
<td>4S, 1994*</td>
<td>4444 Simva 10 to 40</td>
<td>Secondary</td>
<td>Long-term treatment with simvastatin is safe and improves survival in patients with coronary heart disease.</td>
<td>Excluded</td>
<td></td>
</tr>
<tr>
<td>WOSCOPS, 1995*</td>
<td>6595 Prava 40</td>
<td>Primary</td>
<td>Pravastatin significantly reduced the incidence of myocardial infarction and death from cardiovascular causes without adversely affecting the risk of death from noncardiovascular causes in men with moderate hypercholesterolemia and no history of myocardial infarction.</td>
<td>Excluded</td>
<td></td>
</tr>
<tr>
<td>CARE, 1996*</td>
<td>4159 Prava 40</td>
<td>Secondary</td>
<td>The benefit of pravastatin treatment reduced the occurrence of fatal coronary events and nonfatal myocardial infarction in patients with coronary disease who had average cholesterol levels.</td>
<td>Symptomatic CHF excluded</td>
<td></td>
</tr>
<tr>
<td>AFCAPS/TexCAPS, 1998*</td>
<td>6605 Lova 20 to 40</td>
<td>Primary</td>
<td>Lovastatin reduces the risk for the first acute major coronary event in men and women with average cholesterol levels and below average HDL-C levels.</td>
<td>Excluded</td>
<td></td>
</tr>
<tr>
<td>LIPID, 1998*</td>
<td>9014 Prava 40</td>
<td>Secondary</td>
<td>Pravastatin therapy reduced mortality from coronary heart disease and overall mortality, as well as the incidence of all prespecified cardiovascular events in patients with a history of myocardial infarction or unstable angina who had a broad range of initial cholesterol levels.</td>
<td>Symptomatic CHF excluded</td>
<td></td>
</tr>
<tr>
<td>MIRACL, 2001*</td>
<td>3086 Atorva 80</td>
<td>Secondary</td>
<td>Atorvastatin treatment reduces recurrent ischemic events in patients with acute coronary syndromes.</td>
<td>Excluded NYHA IIIb/IV. No difference in worsening heart failure</td>
<td></td>
</tr>
<tr>
<td>MRC/HPS, 2002*</td>
<td>20 536 Simva 40</td>
<td>Secondary</td>
<td>Adding simvastatin to existing treatments safely produces substantial additional benefits for a wide range of high-risk patients, irrespective of their initial cholesterol concentrations.</td>
<td>Severe heart failure excluded</td>
<td></td>
</tr>
<tr>
<td>PROSPER, 2002*</td>
<td>5804 Prava 40</td>
<td>Primary/Secondary</td>
<td>Pravastatin reduced the risk of coronary disease in elderly individuals.</td>
<td>Excluded NYHA III/IV. No difference in CHF hospitalization.</td>
<td></td>
</tr>
</tbody>
</table>
the use of rosuvastatin 10 mg daily, specifically in patients with CHF. Both trials failed to demonstrate a beneficial effect of statin treatment on their primary end point (Table). In addition, a post-hoc analysis of the Heart Protection Study and the CORONA trial revealed a decreased benefit of statin treatment in subjects with higher N-terminal pro-B-type natriuretic peptide levels.18,19 The most recent guidelines on treatment in subjects with higher N-terminal pro-B-type natriuretic peptide levels, lipid levels, and vascular comorbidity in our decision? Or alternatively, do we now have enough evidence to reduce polypharmacy and costs, and possibly further comorbid conditions. We may be in need for a straightforward, randomized trial with patients with CHF testing whether discontinuation of statin treatment is the best practice.

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**Disclosures**

None.

**References**


events with atorvastatin in hypertensive patients who have average or lower-than-average cholesterol concentrations, in the Anglo-Scandinavian Cardiac Outcomes Trial—Lipid Lowering Arm (ASCOT-LLA): a multicentre randomised controlled trial. Lancet. 2003; 361:1149–1158.


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