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).16 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.17 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.13,14 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, 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&lt;sup&gt;1&lt;/sup&gt;</td>
<td>4444</td>
<td>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>
</tr>
<tr>
<td>WOSCOPS, 1995&lt;sup&gt;2&lt;/sup&gt;</td>
<td>6595</td>
<td>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>
</tr>
<tr>
<td>CARE, 1996&lt;sup&gt;3&lt;/sup&gt;</td>
<td>4159</td>
<td>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>
</tr>
<tr>
<td>AFCAPS/TexCAPS, 1998&lt;sup&gt;4&lt;/sup&gt;</td>
<td>6605</td>
<td>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>
</tr>
<tr>
<td>LIPID, 1998&lt;sup&gt;5&lt;/sup&gt;</td>
<td>9014</td>
<td>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>
</tr>
<tr>
<td>MIRACL, 2001&lt;sup&gt;6&lt;/sup&gt;</td>
<td>3086</td>
<td>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>
</tr>
<tr>
<td>MRC/HPS, 2002&lt;sup&gt;7&lt;/sup&gt;</td>
<td>20 536</td>
<td>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>
</tr>
<tr>
<td>PROSPER, 2002&lt;sup&gt;8&lt;/sup&gt;</td>
<td>5804</td>
<td>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>
</tr>
</tbody>
</table>

(Continued)
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 addition, a post-hoc analysis of the Heart Protection Study of statin treatment on their primary end point (Table). In

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progressed beyond a certain threshold in the cardiovascular

preclude the initiation of statin treatment when a patient has

from any cause in older patients with systolic heart failure, although

the drug did reduce the No. of cardiovascular hospitalizations. The

drug did not cause safety problems.

the drug did reduce the No. of cardiovascular hospitalizations. The

drug did not cause safety problems.

significantly reduced the incidence of major cardiovascular events.

significant favorable trend in outcome

an acute coronary event had no significant favorable trend in outcome

results of the GISSI-HF were not taken into consideration

recommendation based on level B evidence.20 However, the

results of the GISSI-HF were not taken into consideration

because they were not available at that time.

Do the results of the CORONA and the GISSI-HF trial preclude the initiation of statin treatment when a patient has progressed beyond a certain threshold in the cardiovascular disease continuum? Should we weigh in causes, 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 is it good clinical practice to discontinue statin treatment in majority of patients with CHF, even of ischemic cause, hyperlipidemia, or with vascular comorbidities? Either way, 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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