Review: β-blockers differ in their efficacy for preventing major cardiovascular events in younger and older patients


Clinical impact ratings: GIM/FP/GP ★★★★★✩✩ Cardiology ★★★★★✩✩

Question
When β-blockers are used as first-line treatment of hypertension, does their efficacy for preventing major cardiovascular events differ between younger and older patients?

Methods

Study selection and assessment: Randomized controlled trials (RCTs) with blinded assessment of outcome that compared β-blockers with placebo or other antihypertensive drugs as first-line therapy for hypertension. 21 RCTs met the selection criteria: 10 trials (n = 50 612) involved younger patients (mean age 46 to 56 y), and 11 trials (n = 95 199) involved older patients (mean age 60 to 76 y).

Outcomes: A composite endpoint of stroke, myocardial infarction (MI), or death; stroke; MI; death; and heart failure.

Main results
In younger patients, β-blockers reduced risk for the composite endpoint more than placebo or other antihypertensive drugs (Table). In older patients, β-blockers did not differ from placebo or other antihypertensive drugs for the individual outcomes of stroke, MI, death, or heart failure. In older patients, β-blockers reduced risk for stroke (relative risk reduction [RRR] 22%, 95% CI 2 to 37) and heart failure (RRR 46%, CI 19 to 63) more than did placebo (groups did not differ for MI or death), but were associated with increased risk for stroke (relative risk increase 18%, CI 7 to 30) compared with other antihypertensive drugs (groups did not differ for MI, death, or heart failure).

β-blockers as first-line treatment of hypertension in preventing the composite endpoint (stroke, myocardial infarction, or death) in younger (mean age < 60 y) and older (mean age ≥ 60 y) patients*

<table>
<thead>
<tr>
<th>Age group</th>
<th>Number of trials (n)</th>
<th>Beta-blockers</th>
<th>Placebo</th>
<th>RRR (95% CI)</th>
<th>NNT (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Younger</td>
<td>3 (19 414)</td>
<td>3.7%</td>
<td>4.3%</td>
<td>14% (1 to 26)</td>
<td>168 (91 to 2342)</td>
</tr>
<tr>
<td>Older</td>
<td>5 (8019)</td>
<td>13%</td>
<td>14%</td>
<td>11% (-- to 25)</td>
<td>Not significant</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Age group</th>
<th>Number of trials (n)</th>
<th>Beta-blockers</th>
<th>Other antihypertensive drugs</th>
<th>RRI (CI)</th>
<th>NNH (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Younger</td>
<td>5 (30 412)</td>
<td>4.9%</td>
<td>5.0%</td>
<td>3% (-- to 12)</td>
<td>Not significant</td>
</tr>
<tr>
<td>Older</td>
<td>7 (79 775)</td>
<td>9.9%</td>
<td>9.4%</td>
<td>6% (1 to 10)</td>
<td>179 (107 to 1069)</td>
</tr>
</tbody>
</table>

*Abbreviations defined in Glossary; weighted event rates, RRR, RRI, NNT, NNH, and CI calculated from data in article using a random-effects model.

Commentary
Some guidelines now state that β-blockers are not preferred initial antihypertensive therapy for patients without other indications (e.g., angina) for their use (1). Others suggest that β-blockers may still be recommended for first-line treatment of hypertension for patients < 60 years of age, presumably based in part on the systematic review by Khan and colleagues (2). All guidelines recommend thiazides as a first-line choice and calcium-channel blockers as an alternative. Another point of controversy is whether the “β-blocker” in this situation really means atenolol, since it was the drug used in most β-blocker hypertension trials.

How does the review by Khan and McAlister help us? Although the review created an age cutoff of 60 years “because the pathophysiology of hypertension differs in older and younger patients,” this notion is contentious. Isolated systolic hypertension is the diagnosis in > 85% of patients > 60 years of age compared with only 25% in those < 50 years, but it is important to note that those 50 to 59 years are a mixed group (3). Furthermore, there is no RCT of hypertension treatment stratified by age to support the notion of differing pathophysiologic mechanisms.

The issue of β-blockers as initial therapy remains unresolved in practice as well. In a review of a Medicaid database from 2001 to 2005, the use of β-blockers as initial therapy remained consistently at 25% in a population of 5373 patients with newly diagnosed hypertension, seemingly uninfluenced by recent guidelines (4). This finding may indicate that physicians have other reasons for prescribing β-blockers (including perseveration), the newer guideline messages have not yet been communicated well, or physicians simply do not “buy” the message.

Robert Weiss, MD
Androscoggin Cardiology Associates
Auburn, Maine, USA

References