Can We Use $\beta$-Blocking Agents in Patients With Peripheral Artery Disease?

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See related article, pp 148–154

Peripheral artery disease (PAD) has been for many years a chapter in cardiovascular diseases that did not attract the interest of clinicians. Intermittent claudication, the most common clinical manifestation of PAD, was considered a rather unimportant symptom. Several new findings published during the last decade have profoundly changed our views on PAD. First, intermittent claudication significantly impacts on the quality of life and on the activities of the patients experiencing it. Moreover, and at least as important, a number of large-scale studies and registries unraveled severely increased risk for coronary and cerebrovascular morbidity and mortality in PAD patients. In fact, this should not surprise us, because the most frequent cause of PAD is, by far, atherosclerosis. The increased risk is of particular importance, because many patients with proven PAD are completely asymptomatic. In such cases, PAD is only detected by clinical examination (absent peripheral pulses) or by measuring ankle brachial pressure index. Whichever way they are detected, the increased risk is present whether the disease is symptomatic or not. Therefore, with all of this in mind, physicians and scientists alike start to realize that PAD should be seen not only as a local problem but also as a marker of atherosclerosis elsewhere in the body.

As a consequence, treatment of PAD patients should be oriented at symptoms, if present, but above all, at controlling total CV risk (Table). Symptoms of intermittent claudication are best treated with regular training and smoking cessation; pharmacological approach by drugs like cilostazol or naf-tidrofuryl can further improve claudication distance. Total risk is controlled by adaptation of lifestyle and antiplatelet therapy. Hypertension often is associated with PAD; systolic hypertension is especially highly prevalent in PAD patients, most likely because of stiffening of the large arteries. Thus, antihypertensive drugs will be necessary in many PAD patients. There is no convincing evidence of superiority of one antihypertensive drug over another with respect to controlling hypertension in PAD patients or affecting their claudication distance. Slightly better results are obtained by ACE inhib-
Table. Management of Hypertension in Patients With Peripheral Artery Disease

<table>
<thead>
<tr>
<th>Intermittent Claudication*</th>
<th>Management of</th>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Total Cardiovascular Risk</td>
<td>Hypertension</td>
<td></td>
</tr>
<tr>
<td>Lifestyle adaptation</td>
<td>Lifestyle adaptation</td>
<td>Lifestyle adaptation</td>
<td>(Eating habits)</td>
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<tr>
<td>Regular training</td>
<td>Antiplatelet therapy</td>
<td>Antihypertensive drugs:</td>
<td></td>
</tr>
<tr>
<td>Stop smoking</td>
<td>All classes acceptable;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drug treatment (cilostazol, nafldifuroyl, etc)</td>
<td>Arguments in favor of: β-Blocking agents</td>
<td>Angiotensin-converting enzyme inhibitors</td>
<td></td>
</tr>
</tbody>
</table>

*Many patients are asymptomatic.

Nebivolol did significantly better than metoprolol with respect to initial pain, that is, first pain when walking on the treadmill. Absolute claudication distance was similar for both drugs. In general, initial claudication pain responds better to any drug therapy than the absolute distance where maximal ischemia is urging the patient to stop walking. The greater improvement with nebivolol than with metoprolol on initial pain may well be relevant in daily life, because patients most often stop when claudication pain starts; they rarely pursue walking until maximal pain in contrast to what is done on the treadmill in the clinic. It would be interesting to confirm such findings using tools like claudimeters, which are able to measure the number of steps or the distances walked by the patient in their normal environment. The treadmill is considered a reliable and objective tool to measure walking distance, but it still is, to some extent, artificial and not always similar to what patients experience in normal life.

β-Blockade could even be indicated to treat hypertension in PAD patients. As mentioned above, PAD patients have a clearly increased risk to develop coronary atherosclerosis and to experience the events secondary to it. β-Blockers could be indicated because they seem to protect coronary patients against the complications of the disease.

This reasoning should be kept in mind when writing new guidelines on the treatment of hypertension and focusing on special categories of patients.

Treatment of hypertension in PAD patients is a complex issue (Table). One needs to convince the patients and their families that strict control of the elevated blood pressure is essential; β-blockers in light of the present study and ACE inhibitors (see above) may well take a privileged position in this respect. Still, studies with head-to-head comparison of the different antihypertensive drugs available are badly needed. However, on top of blood pressure, the strongly increased risk to develop cardiovascular morbidity and mortality should be highlighted; to this extent, lifestyle adaptation and platelet inhibition play essential roles. All of the clinicians taking care of PAD patients with hypertension should devote their best efforts to the management of this special category of patients.

In any case, the results of the present study bring another piece of evidence that β-blocking agents can indeed be used in patients with stable PAD. Moreover, because first claudication pain was postponed in the patients randomized to nebivolol, β-blockers with vasodilating capacity may be preferred.

Disclosures

None.

References

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