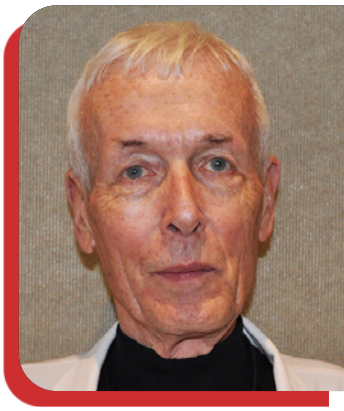
# PERSPECTIVES ON RECENT STUDIES IN HYPERTENSION

## Beta-Blockers upgraded for Hypertension – the bad, the ugly, and the not so good



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In June of this year the European Society of Hypertension (ESH) issued new guidelines for the management of hypertension.[1] In this document, Beta-Blockers (BBs) as a class were upgraded and put on an equal footing with thiazide diuretics, renin–angiotensin system blockers (e.g., angiotensin receptor blockers, angiotensin-converting enzyme inhibitors), and calcium channel blockers. In contrast, most other guidelines advise that BBs should be used for specific guideline-directed indications only.

This unexpected move sparks a few simple questions and considerations:

1. Was this upgrade evidence-based or convenience-based?

   The authors of the ESH guideline freely admit that there is no new evidence for this move. Hence it must have been solely based on convenience. The simple but important question here is of course, convenience for who? In this context, we should recall that some fixed combinations of BBs with other drugs have recently become available. To even remotely suspect that this in any way has been related to the upgrade seems utterly preposterous.

2. The BBs lower brachial BP largely by reducing cardiac output. However, when BP-reducing effect of BBs was concomitantly assessed both on brachial artery and centrally (in the aorta), the reduction in the latter was on average more than 4 mm Hg less pronounced.[2] Population-wise, such difference can translate into a lesser risk reduction by 5-12%.[3] Little surprise that BBs have been documented to be less efficacious than other drug classes to prevent the risk of stroke.[4]

3. The use of BBs comes at a price. Even though a recent meta-analysis purported not to demonstrate any increase in depression fatigue or sexual dysfunction when treated with BBs[5], a reanalysis of the same data showed a 2 to 5 times higher withdrawal rates in BB patients due to sexual dysfunction or fatigue, compared with placebo. For every event prevented, three patients experienced impotence due to BBs. In an another eight, fatigue resulted in withdrawal from such therapy.[6] For an asymptomatic disease such as essential hypertension, such an appalling risk-benefit ratio begs for second thoughts.

4. Today, the advice to use a particular drug class or a particular medication is driven by the outcomes in randomized clinical trials. BBs have been consistently shown to be less efficacious in preventing major outcomes, especially stroke, when compared to ACEi/ARBs or CCBs.[7,8,9] To some extent the guideline authors based their decision to upgrade BBs on a network meta-analysis.[10] However, a closer look at this meta-analysis showed that BBs had no effect on cardiovascular mortality and reduced stroke between 35% and 49% less well than did CCBs, ACEIs, ARBs, and thiazides, respectively. If anything, this meta-analysis corroborates that BBs should keep their downgraded status as most other recent national and international guidelines indicate.

5. There is no doubt that BBs may offer some benefits in many conditions coinciding with hypertension. As underlined by the ESH guidelines, more than 50 such "twofer indications" can be found, ranging from post myocardial infarction (with weak evidence at

best), to heart failure (strongest evidence). It may appear attractive, convenient and less expensive to do a BB twofer, i.e. to lower BP and to concomitantly confer cardioprotection in a post-MI patient. However, the post-MI patient has also been documented to be at an excessively increased risk of stroke (30-fold for the first month and 3-fold for the first year).[11] To us it seems irresponsible to lower BP with a drug class that has a track record of little if any efficacy in reducing the risk of stroke. If indicated, the post-MI patient certainly should receive a BB, but for hypertension an evidence-based therapeutic strategy should be selected that will not only lower mmHg but also, and more importantly confer cerebroprotection. Lowering BP with generically available drug classes such as CCBs, renin–angiotensin system blockers, and long-acting thiazides has been shown to grant outstanding stroke protection. Rather than for convenience's sake to pursue a BB twofer and put the patient at risk, evidence-based therapy should be prescribed.

6. Undoubtedly, the bad, the ugly and the not so good of BBs mostly originated from studies done with atenolol. The argument goes that newer BBs such as carvedilol, nebivolol etc. are different in that they exhibit a more favourable hemodynamic and metabolic profile. True, but then;

a) there are no outcome studies with the newer BBs in hypertension and

b) the ESH guidelines have upgraded all BBs, including atenolol.

As stated, in the ESH guidelines, there is no new evidence justifying a BB-upgrade to first-line therapy. We are concerned that this move might lead to widespread harm because of inferior stroke protection.[12]

It has been said that guidelines in medicine are merely created to offer ammunition to lawyers and to prevent doctors from thinking. Contrary to this dictum, the unexpected upgrade of BBs by the ESH guidelines should enliven physicians to think again and perhaps to more than ever remember Hippocrates's precept of first do not harm.

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