HTN Guidelines Favor Combination Therapy for HTN Management

Written by Toni Rizzo

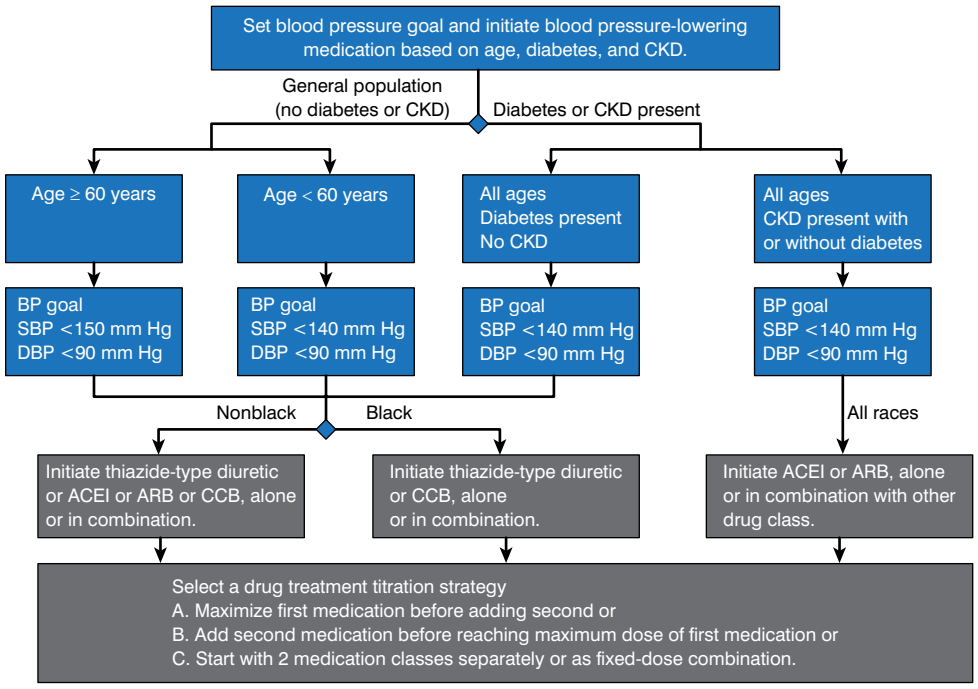
Alistair Hall, MD, Leeds Institute of Cardiovascular and Metabolic Medicine, Leeds, United Kingdom, reminded the audience that blood pressure (BP) is a surrogate that is treated to prevent cardiovascular disease (CVD) and its consequences. However, outside of clinical trials, it is difficult to know how these outcomes are affected by antihypertensive therapy. Although clinical trials provide useful information, they do not give the full picture. Real-life practice is more complicated than clinical trials, but both need to be considered in managing hypertension (HTN).

New international guidelines for the management of HTN were issued in Europe and the United States in 2013. Both the American Society of Hypertension and the International Society of Hypertension guidelines attempted to be practical but were criticized as opinion pieces that were not developed using a formal guideline process [Weber MA et al. *J Clin Hypertens* 2013]. The Eighth Joint National Committee (JNC 8) guidelines claimed to be a scientific advisory document but were criticized for being excessively stringent [James PA et al. *JAMA* 2013]. According to Prof. Hall, the European Society of Hypertension (ESH) and European Society of Cardiology (ESC) guidelines allow for clinical opinion [Mancia G et al. *Eur Heart J* 2013]. All 3 sets of guidelines agree that the recommendations are not a substitute for clinical judgment.

The JNC 8 algorithm for the management of high BP recommends initiating treatment with monotherapy and adding a second medication before reaching the maximum dose of the first antihypertensive (Figure 1).

The ESH/ESC guidelines recommend any of the drug classes for monotherapy (Table 1) [Mancia G et al. *Eur Heart J* 2013]. This recommendation is supported by a meta-analysis on the use of antihypertensive drugs for preventing CVD [Law MR et al. *BMJ* 2009]. The most robust evidence supports using angiotensin-converting enzyme inhibitors (ACEIs), calcium channel blockers (CCBs), and nonthiazide diuretics for prevention of CVD and all-cause death. ACEIs have consistently been shown to prevent death from all causes, while

Figure 1. JNC8 Algorithm for the Management of High BP in Adults



ACEI=angiotensin-converting enzyme inhibitor; ARB=angiotensin receptor blocker; BP=blood pressure; CCB=calcium channel blocker; CKD=chronic kidney disease; DBP=diastolic blood pressure; SBP=systolic blood pressure.

Reproduced from James PA et al. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). *JAMA*. 2014;311(5):507-520. With permission from the American Medical Association.

Table 1. ESH/ESC Guidelines for Medical Management of HTN

Recommendations	Class	Level
Diuretics (thiazides, chlorthalidone, and indapamide), BBs, calcium antagonists, ACEIs, and ARBs are all suitable and recommended for the initiation and maintenance of antihypertensive treatment, either as monotherapy or in some combinations with one another.	I	A
Some agents should be considered as the preferential choice in specific conditions because used in trials in those conditions or because of greater effectiveness in specific types of OD.	IIa	C
Initiation of antihypertensive therapy with a 2-drug combination may be considered in patients with markedly high baseline BP or at high CV risk.	IIb	C
The combination of 2 antagonists of the RAS is not recommended and should be discouraged.	III*	A*
Other drug combinations should be considered and probably are beneficial in proportion to the extent of BP reduction. However, combinations that have been successfully used in trials may be preferable.	IIa	C
Combinations of 2 antihypertensive drugs at fixed doses in a single tablet may be recommended and favored, because reducing the number of daily pills improves adherence, which is low in patients with HTN.	IIb	B*

ACEI=angiotensin-converting enzyme inhibitor; ARB=angiotensin receptor blocker; BB=β-blocker; BP=blood pressure; CV=cardiovascular; ESC=European Society of Cardiology; ESH=European Society of Hypertension; HTN=hypertension; RAS=renin-angiotensin system.

Reproduced from Mancia GR et al. 2013 ESH/ESC guidelines for the management of arterial hypertension. *Eur Heart J.* 2013;31(7):1281-1357. With permission from Oxford University Press.

*On November 12, 2014, the colors in these cells were edited.

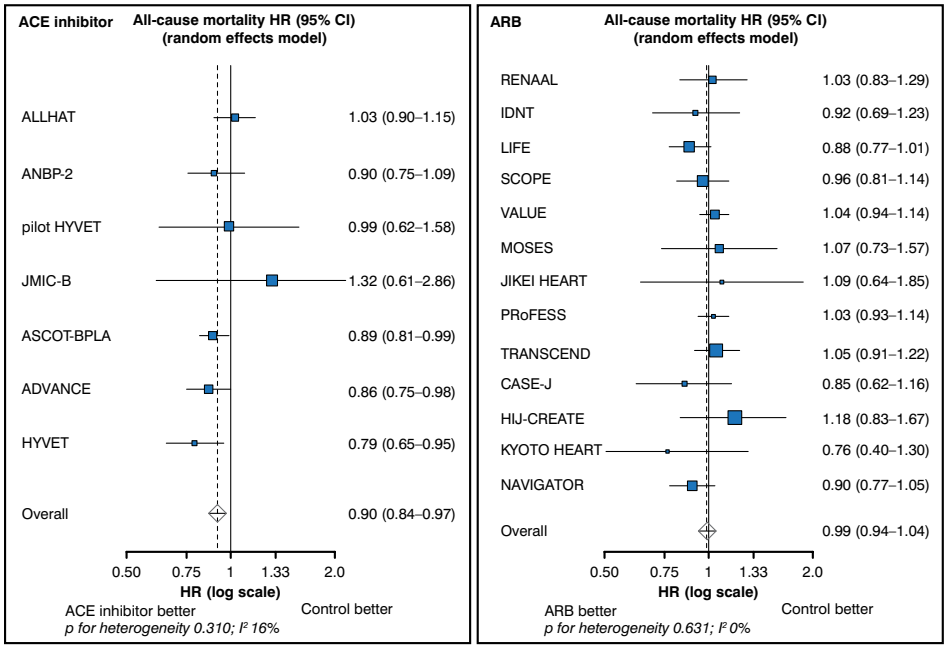
angiotensin receptor blockers have demonstrated no all-cause mortality reduction and in some cases have been associated with an excess of mortality from myocardial infarction (Figure 2) [van Vark LC et al. *Eur Heart J* 2012; Strauss MH, Hall AS. *Circulation* 2006].

The ESH/ESC guidelines recommend adding second and third drugs when the BP target is not achieved. The use of fixed-combination therapy is supported [Gupta AK et al. *Hypertension* 2010], with emphasis on choosing a drug combination on the basis of trial success. ACEI–nonthiazide diuretics combinations (eg, indapamide and perindopril) and ACEI-CCB combinations (eg, benazepril and amlodipine) have been shown to prevent death from all causes [Jamerson K et al. *N Engl J Med* 2008; Patel A. *Lancet* 2007].

For elderly patients with systolic BP (SBP) ≥ 160 mm Hg, the ESH/ESC guidelines recommend reducing SBP to between 140 and 150 mm Hg. Antihypertensive treatment may be considered in fit elderly patients aged < 80 years with SBP ≥ 140 mm Hg if treatment is well tolerated.

Prof. Hall concluded that the HTN guidelines highlight the need for combination therapy, particularly with an ACEI plus a CCB. The evidence favors the ACEI perindopril, the CCB amlodipine, and the diuretic indapamide.

Figure 2. Prevention of All-Cause Mortality: ACEIs and ARBs



ACEI=angiotensin-converting enzyme inhibitor; ARB=angiotensin receptor blocker.

Reproduced from van Vark LC et al. Angiotensin-converting enzyme inhibitors reduce mortality in hypertension: a meta-analysis of randomized clinical trials of renin-angiotensin-aldosterone system inhibitors involving 158 998 patients. *Eur Heart J.* 2012;33(16):2088-2097. With permission from Oxford University Press.