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Blood pressure classification and values to treat

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Abstract: Blood pressure (BP) values can be classified in two ways, ie, either based on the relationship between BP and cardiovascular risk, or on threshold values at which antihypertensive drugs are indicated for blood-pressure lowering, as shown by randomized outcome trials. As there are substantial differences between the two classifications, this can be confusing, especially for the patient. Current hypertension guidelines do not entirely clarify this. ■ *Heart Metab*. 2019;79:5-9

Keywords: antihypertensive drug; blood pressure; cardiovascular risk; hypertension

Introduction

Classification of blood pressure (BP) values relies on two different criteria, one based on the relationship between BP and cardiovascular (CV) risk and the other on the values at which BP lowering with antihypertensive drugs is indicated, based on evidence from randomized outcome trials. Because the two classifications differ substantially, this not infrequently generates confusion, especially for the patient, which is not entirely resolved by current hypertension guidelines.[1,2]

Classification based on the relationship between BP and CV risk

Epidemiological data agree that in the general population BP correlates positively with the incidence and risk of CV outcomes, a relationship which is progressive for systolic and diastolic values above 110 to 115 mm Hg and 70-75 mm Hg, respectively.[3-5] This holds true for all major CV outcomes (myocardial infarction, stroke, heart failure) [6,7] as well as for fatal and nonfatal CV events; the increased risk of fatal events even extends to all-cause mortality.[3-5] A similar relationship also holds for BP and major renal outcomes, such as renal insufficiency, need for dialysis, and kidney transplantation.[8] Thus, from an epidemiological perspective, the lower the BP, the lower the individual's risk; which at the population level justifies the adoption of lifestyle changes that favor BP reduction, such as restriction of salt intake, encouraging exercise, more vegetable-based diets, antismoking campaigns, etc. Widespread implementation of these measures, however, has so far almost invariably turned out to be difficult. Indeed, compared with historical data, no substantial BP reduction has been reported in the worldwide population. On the contrary, BP values have been shown to have increased in the largely represented medium or low-income countries,[9] leading to the prediction that in 10 to 20 years hypertension will be noticeably more prevalent than it is today, affecting perhaps more than half of the elderly population.[10]

Despite its continuous nature, the relationship between BP values and CV risk is customarily subdivided into different categories, the aim being to make doctors' perception of subjects' risk easier and more

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immediate. The most popular BP classification is the one generated by the 7th US Joint National Committee Guidelines in 2003,[11] which has been adopted by European guidelines, including the recent ones published in 2018 *(Table I).*[1] Paradoxically, a major departure from this classification has been proposed by the US in their recent guidelines, which have: i) reduced the BP threshold at which a BP increase can be termed "hypertension" from 140/90 mm Hg to 130/80mm Hg; and ii) lowered the value at which BP can be defined as elevated to >120/80 mm Hg, regardless of the subject's age (*Table I*, right section).[2] This has generated widespread disagreement and debate, particularly because in older subjects defining a systolic BP ≥120 mm Hg as elevated, means that virtually the whole elderly population is affected.

BP (mm Hg)	2003	2017
<120/80	Normal	Normal
120-129/80-84	Prehypertension	Elevated
130-139/85-89		Grade 1 HT
140-159/90-99	Grade 1 HT	Grade 2 HT
160-179/100-110	Grade 2 HT	
>180/110	Grade 3 HT	

Table I *Classification of blood pressure (BP) values in the US hypertension (HT) guidelines issued in 2003 and 2017.*[2,11]

Classification based on randomized outcome-based trials

The decision to start antihypertensive drug treatment cannot be based on the abovementioned epidemiological data because of the need to additionally prove that, at any given BP value, a BP-lowering intervention is associated with a reduction of CV outcomes or that, in the words of the famous epidemiologist J. Rose, the therapeutic intervention "does more good than harm." Over the last 50 years this has been demonstrated for progressively lower initial BP values, which have led to the recommendation that antihypertensive drugs be used at progressively lower pressures: historically this was a systolic BP greater than 180, later 160 mm Hg (grade 2 and 3 hypertension) and then for patients with grade 1 hypertension, ie, with a BP in the 140 to 159 mm Hg systolic and 90 to 99 mm Hg diastolic BP range, if accompanied by a high CV risk.[12] In the latest 2018 European guidelines antihypertensive drug treatment is recommended in patients with grade 1 hypertension even when their CV risk is only low to moderate because: i) the HOPE-3 trial has shown that in these patients a two-drug antihypertensive regime significantly lowers the risk of CV outcomes[13]; and ii) this has been confirmed by a meta-analysis of randomized trials, which has shown that in low-risk grade 1 hypertension, treatment capable of reducing systolic and diastolic BP by approximately 7/5 mm Hg significantly reduces all hypertension-related CV morbid or fatal events *(Figure 1).*[14] Most importantly, the recommendation to reduce BP by antihypertensive drug

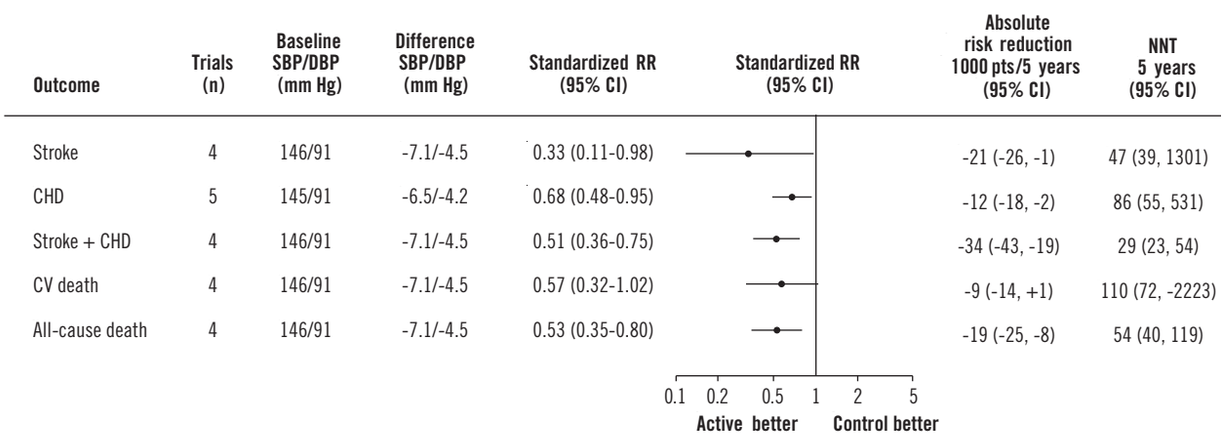

Figure 1 *Effect of systolic and diastolic blood pressure (SBP and DBP) reduction by drug treatment in trials involving patients with grade 1 hypertension and a low-to-moderate cardiovascular (CV) risk.*
RR, relative risk; CHD, coronary heart disease; CI, confidence interval; NNT, number of events saved by treating 1000 patients for 5 years. Effects of treatment were calculated for a BP reduction of 10/5 mm Hg.
Reproduced from ref 14: Thomopoulos C, Parati G, Zanchetti A. Effects of blood pressure lowering on outcome incidence in hypertension: 2. Effects at different baseline and achieved blood pressure levels--overview and meta-analyses of randomized trials. J Hypertens*. 2014;32(12):2296-2304. Copyright © ISH/ESH 2014*

treatment has been extended to grade 1 elderly hypertensive patients; based on the evidence from three pooled trials (HDFP, HOPE, PATS =8389) that in grade 1 hypertensive patients aged >60 years, BP reduction was accompanied by clear-cut and marked reductions in outcomes: CV death by 45%; all-cause death by 21%; and CV events by 42%.[15] At present, in the very elderly (patients aged ≥80 years) the BP threshold for drug treatment remains higher, ie, a systolic BP ≥160 mm Hg, since at this more advanced age the only available evidence remains that provided by the HYVET trial in which patients were recruited only if their systolic BP was ≥160 mm Hg.[1]

Whether antihypertensive drug treatment should be extended to patients with a BP <140/90 mm Hg has received a different answer in different guidelines, as well as by the same guidelines in different years! There is a general agreement that subjects with high normal BP values, ie 130 to 139/85 to 89 mm Hg *(Table I)* have a noticeable increase of CV risk compared with subjects with a lower BP value,[16] with in addition a much greater risk of later developing frank hypertension.[17] Evidence is limited and inconsistent, however, on whether under these circumstances a BP-lowering intervention is beneficial. In 2007, for example, the European guidelines advised lowering BP by antihypertensive drugs if the CV risk of patients with a high normal BP was high, such as when hypertension coexists with diabetes.[18] In contrast, in 2013, the same guidelines have excluded any use of antihypertensive drugs in patients with a BP within this range.[12] While in 2018 they have restricted drug treatment to patients with a very high CV risk *(Figure 2)* because of evidence from a meta-analysis of randomized trials that, in patients with a high normal BP, a BP reduction was accompanied by a reduction of stroke only if there was a history of CV events.[19] US guidelines agree with the European guidelines that only some patients in this BP range need drug treatment.[2] Based on the results of the SPRINT[20] trial as well as on a large network meta-analysis,[21] the US guidelines identify these patients as those with a CV risk >10% (chance of an event within 10 years). This is a much larger fraction of the population than that considered in the European guidelines, since a CV risk ≥10% is common in both elderly males and females in whom a BP between 130 to 139/85 to 89 mm Hg is highly prevalent. The European guidelines[1] consider the evidence behind this recommendation as questionable, also because in the SPRINT trial baseline BP values were in the high normal BP range as a result of antihypertensive treatment at enrolment (in most instances with two drugs), which suggests that the majority of patients originally had frank hypertension, rather than high normal pressures. Furthermore, network meta-analyses are based on nonrandomized comparisons,[1] which reduces the scientific strength of their results.

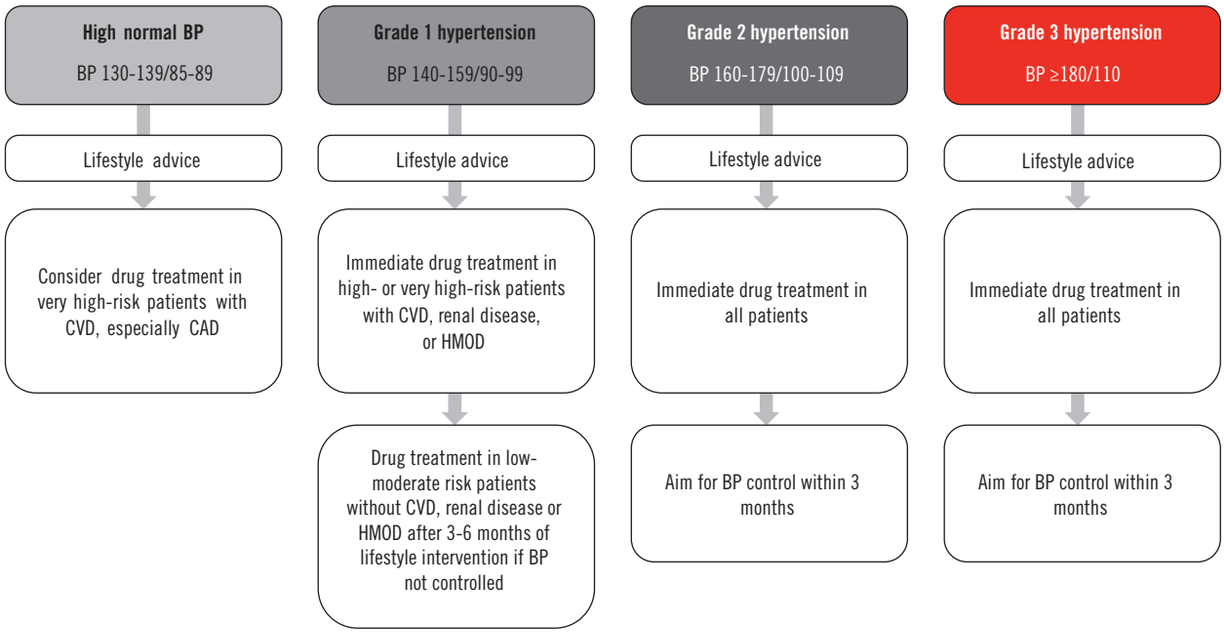

Figure 2 *Blood pressure (BP) values at which to initiate antihypertensive drug treatment in the 2018 European guidelines.[1]*

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Initial antihypertensive drug treatment – BP or CV risk criteria?

In patients with grade 2 or 3 hypertension CV risk is almost invariably close to or in the high range, this being the case also in most hypertensive patients with an advanced age. In contrast, in younger patients with grade 1 hypertension CV risk may range from a low/moderate to high/very high, which has for years raised the question whether a decision on treatment implementation should be based on their risk level or just on their mild BP elevation. As mentioned above, recent evidence has shown that in grade 1 hypertension BP-lowering treatment leads to patient protection regardless of the CV risk, making BP criteria the main decision factor. Evidence has also been obtained against the argument that, because it saves more events, treatment of a high CV risk condition can be more cost-effective than treatment of a low risk condition.[22] In a meta-analysis of trials on hypertensive patients with different risk levels, the number of events saved by BP-lowering interventions was progressively greater as the patient's risk increased. This was more than counterbalanced, however, by a disproportionally greater increase of the residual risk *(Figure 3),* indicating that limiting treatment of high- or very high-risk hypertensive individuals denies effective CV protection to a large number of patients, with a strong negative impact on overall costs.[23] This offers strong support to early antihypertensive treatment, ie, when risk is still low to moderate and the phase of risk irreversibility has not yet been reached. ■

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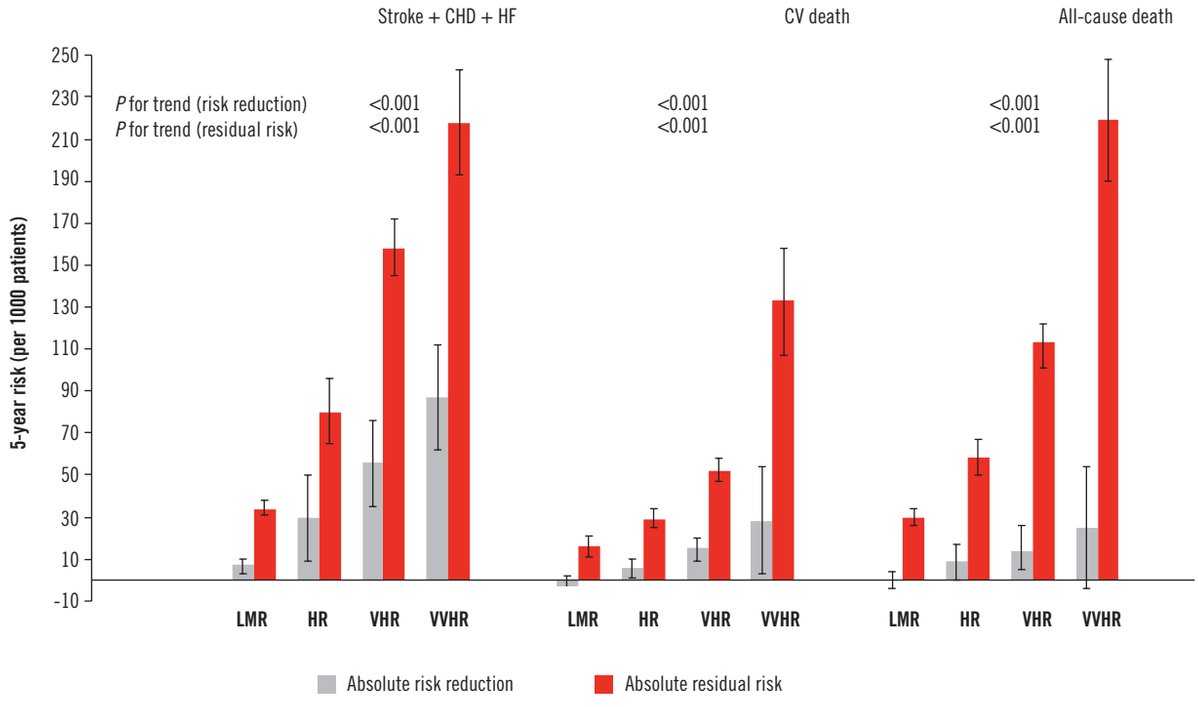

Figure 3 *Absolute cardiovascular (CV) risk reduction by a BP reduction of 10/5 mm Hg (systolic/diastolic). Data for CV events, CV death and all-cause death. Concomitant effects on residual CV risk are also shown.*
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