

A LOWER BLOOD PRESSURE TARGET IN HYPERTENSIVE PATIENTS: UPDATE ON THE RECENT HYPERTENSION GUIDELINES

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Using a threshold of 140/90 mm Hg, the global prevalence of hypertension is estimated to be over 1 billion.¹ Elevated BP is the leading cause of death and disability-adjusted life years worldwide.² While it has long been demonstrated that a reduction in elevated BP decreases the risk of death and cardiovascular events,³ the optimal BP target remains a matter of debate.

Most hypertension guidelines issued from 2011 to 2015 agreed on a threshold of 140/90 mm Hg both to define hypertension and as a treatment target. The ACC/AHA guidelines on high BP,⁴ issued in 2017, generated a worldwide debate by lowering the threshold defining hypertension and the treatment target, from 140/90 to 130/80 mm Hg. The 2018 ESC/ESH guidelines for the management of arterial hypertension⁵ kept the definition of hypertension above 140/90 mm Hg, but recommended a target of 130/80 mm Hg, in line with the American guidelines.

We will give a brief overview on these recent guidelines, with a focus on the thresholds for hypertension definition, treatment initiation, and treatment target. We will discuss the underlying evidence for these new guidelines, and the reasons why clinicians are not unanimously convinced they should apply a lowered threshold in daily practice.

DEFINITION OF HYPERTENSION

A major change in the 2017 American guidelines was the replacement of the decades-old 140/90 mm Hg threshold defining hypertension with a new lower threshold: 130/80 mm Hg. A systolic BP of 130–139 or a diastolic BP of 80–89 now defines stage 1 hypertension, while any values above 140/90 mm Hg define stage 2 hypertension. This new definition increased the estimated prevalence of hypertension in the US from 32% to 46%,⁶ and generated heated controversies.

In this context of strong intellectual stances by hypertension experts, the much-awaited European guidelines, issued in the summer of 2018, maintained

the hypertension definition unchanged from the previous 2013 guidelines: a systolic BP of 130–139 and/or a diastolic BP of 85–89 define a “high-normal” BP, while grade 1, 2, and 3 hypertension are defined by a systolic BP/diastolic BP of 140–159/90–99, 160–179/100–109, and $\geq 180/\geq 110$ mm Hg, respectively.

TREATMENT TARGET AND TREATMENT THRESHOLD

The American guidelines lowered the BP target to below 130/80 mm Hg for all patients, with important considerations on how to reach this lower target. In all treated patients, treatment should be intensified to reach 130/80 mm Hg. In previously untreated patients with systolic BP between 130 and 139 mm Hg or diastolic BP between 80 and 89 mm Hg, only those with or at high risk for cardiovascular disease (including those ≥ 65 years old) should be treated pharmacologically. In the large majority of the patients newly diagnosed with hypertension, nonpharmacological therapy alone is recommended.

The European guidelines, in line with the American guidelines, also lowered BP targets for most patients: the treatment goal for systolic BP should be 130 mm Hg “or lower, if tolerated” in most patients (with the exception of patients with chronic kidney disease and patients ≥ 65 years, for whom the target is 130–139 mm Hg). The diastolic BP target was lowered to below 80 mm Hg for all patients. Importantly, treatment initiation remained at 140/90 mm Hg for most patients, but it was extended to patients with “high-normal” BP (as defined above) who are at very high risk, “especially those with coronary artery disease.”

Noteworthy, because of the differences in the thresholds defining hypertension, the initiation of pharmacological treatment, and the treatment target, the major difference in the definition of hypertension between the American and European guidelines does not actually translate into a major difference in the clinical management of patients. Indeed, on the one hand, the US guidelines recommend pharmacological treatment for patients with BP 130–139/80–89 mm Hg (grade 1 hypertension) only when they are at high cardiovascular risk, and, on the other hand, the European guidelines recommended to “consider drug treatment” in very high-risk patients with a BP of 130–139/85–89 mm Hg (“high-normal BP”). For all treated patients (except patients ≥ 65 years old or with chronic kidney disease), the common new target is 130/80 mm Hg. A remaining subtle difference is the threshold of diastolic BP for drug initiation in high-risk patients (80 vs 85 mm Hg).

UNDERLYING EVIDENCE FOR LOWER BP TARGETS

The rationale for more-intensive treatment in high-risk patients is the greater absolute risk reduction as baseline cardiovascular risk increases.⁷ The lowered threshold of 130/80 mm Hg largely results from the reduced rate of cardiovascular events observed in the intensive treatment arm of the SPRINT trial and from

several recent large meta-analyses showing that intensive BP lowering was associated with decreased cardiovascular events.^{8,9} In SPRINT, 9361 patients with baseline systolic BP higher than 130 mm Hg who were at high cardiovascular risk, but without diabetes or previous stroke, were randomly assigned to standard (<120 mm Hg) or intensive (<140 mm Hg) BP-lowering treatment. The trial was stopped early after a median follow-up of 3.3 years because of a significant 25% reduction in the primary composite outcome and a 27% reduction in mortality.

However, patients in SPRINT were carefully followed-up in the setting of a randomized trial and BP values were measured under unattended conditions to minimize any white-coat effect, but may underestimate casual BP values by 10 to 15 mm Hg. Therefore, the guideline committees advocated for a target BP of 130 mm Hg and not 120 mm Hg as in the SPRINT trial. In addition, these considerations led hypertension experts to warn that the SPRINT target, if translated into community practice, may have deleterious effects because the same targets obtained in routine clinical practice would potentially lie within the left part of the so-called “J-curve,” where excessive BP lowering may be harmful.

TREATMENT INITIATION FOR PATIENTS WITH CORONARY ARTERY DISEASE

Patients with established coronary artery disease are clearly a high-risk group in which earlier treatment initiation is recommended by both guidelines. As a result of the new guidelines, patients with coronary artery disease so far considered as normotensive, should now be treated to reach a BP below 130/80 mm Hg. However, the benefits of a more-intensive BP control have not been consistently observed for patients with coronary artery disease.

In this context, we analyzed data from nearly 6000 patients with coronary artery disease and no history of hypertension (BP <140/90 mm Hg) from the CLARIFY registry.¹⁰ CLARIFY is a large, international, prospective cohort that included 32 703 patients with stable coronary artery disease in 45 countries, with a 5-year follow up. The results showed that a systolic BP above 130 mm Hg was not associated with an increased risk of mortality or cardiovascular events (myocardial infarction or stroke) compared with patients whose blood pressure was optimal according to the recent guidelines, ie, 120–129 mm Hg. In contrast, a diastolic BP above 80 mm Hg was associated with an increased risk compared with 70–79 mm Hg. These results do not support the new systolic threshold of 130 mm Hg for patients with coronary artery disease, but are in favor of a lower diastolic BP target, below 80 mm Hg.

Overall, in the absence of dedicated studies for patients with coronary artery disease, this new 130/80 mm Hg target and treatment threshold is not evidence-based in this population, and clinicians are not unanimously convinced they should apply this lowered threshold in daily practice.

LOWER SAFETY BOUNDARIES

Aside from the similarities in both guidelines highlighted above, the European guidelines introduced a major novelty compared with both previous European and US guidelines, namely lower safety boundaries, at 120/70 mm Hg. The European guidelines defined target ranges rather than just upper limits of BP targets. The target range for systolic BP is 120–130 mm Hg for patients younger than 65 and 130–139 mm Hg for patients older than 65, while the diastolic BP target range is 70–79 mm Hg for all patients.

This word of caution against excessive lowering of BP relies on several observational studies, including a study from our team conducted on the CLARIFY registry in 2016.¹¹ In 22 672 patients treated for hypertension, we showed that achieved systolic BP <120 mm Hg and achieved diastolic blood pressure <70 mm Hg were both associated with a marked increased risk of mortality, myocardial infarction, and hospitalization for heart failure, independently of potential confounding factors. The concern of a “J-curve” is particularly relevant for patients with coronary artery disease because a low diastolic BP may compromise myocardial perfusion, but an increased risk at low BP values was observed in many other populations, and the lower safety boundaries of the European guidelines apply to all treated patients.

Of note, targeting optimal BP ranges for both components of BP will yield situations when clinicians will have to prioritize whether they should aim for an optimal systolic BP or an optimal diastolic BP. In the CLARIFY registry, of the 27 310 patients requiring antihypertensive drug treatment according to recent guidelines, such discordance between systolic and diastolic BP values with regards to their respective targets is observed in half of the patients.¹² As data to guide the optimal strategy when BP components are dissociated are lacking, the recent European guidelines highlight another remaining gap in evidence and that the saga of the BP targets is not over.

CONCLUSION

In conclusion, largely influenced by the results of the SPRINT trial, recent hypertension recommendations advocated for a more intensive treatment in hypertensive patients and for an earlier initiation of pharmacological treatment in high-risk patients. Improving global BP control with a target below 140/90 mm Hg is an indisputable public health priority, but the expected risk/benefit ratio of a reinforced treatment to reach less than 130/80 mm Hg for all patients remains uncertain. ■

Conflicts of interest

The author declares support for congress registration from Servier.

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