

Target blood pressure for antihypertensive treatment

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In 2007 the guidelines on hypertension of the European Society of Hypertension (ESH) and the European Society of Cardiology (ESC) [1] recommended antihypertensive treatment to reduce blood pressure to less than 140/90 mmHg but also to target a lower blood pressure value, i.e. less than 130/80 mmHg in patients defined as being at high cardiovascular risk because of diabetes, a history of coronary disease or a history of cerebrovascular disease. However, a subsequent reappraisal of the randomized trial evidence on which these recommendations were based [2] led the 2013 ESH/ESC guidelines to introduce a substantial modification. Because in either low-to-moderate and high cardiovascular risk patients major randomized clinical trials did not show blood pressure reductions to less than 130/80 mmHg to increase the benefit obtained by reducing blood pressure to less than 140/90 mmHg, the latter was recommended as a unified blood pressure target for antihypertensive treatment, regardless the level of risk [3]. Furthermore, because in patients aged 60 years or more the treatment-related benefit had been shown for systolic blood pressure values between 140 and 150 mmHg, this higher target was indicated as the most evidence-based one in elderly hypertensive individuals [3]. The same blood pressure targets were few months later recommended by hypertension guidelines issued in United States [4] as a follow-up of those pub-

lished in 2003 with the endorsement of the US Joint National Committee [5]. For both European and American medical practice this represented not just a marginal but an important shift of the treatment strategy in a conservative direction because hypertensives in whom cardiovascular risk is high are by no means a small fraction of the overall hypertensive population [6]. Furthermore, high blood pressure has its maximal prevalence in the elderly [7] in whom relaxing previous higher blood pressure targets thus has major implications for medical routine.

Identification of the target blood pressure at which the benefit of antihypertensive treatment is maximized remains an unfinished business, however, as exemplified by the recently released results of the Systolic Blood Pressure Intervention trial (SPRINT) [8, 9]. In this trial hypertensive patients aged 50 years or more in whom cardiovascular risk was high were randomized to achieve a systolic blood pressure of 140 mmHg or 120 mmHg, the purpose being to determine whether in those more aggressively treated cardiovascular and renal events were more effectively prevented. As detailed in a press release (so far the only available source of information), after almost three years of treatment the trial was stopped because the incidence of overall cardiovascular morbidity and mortality (heart failure, stroke and myocardial infarction) was about one third less in the lower systolic blood pressure group, which also showed an about 25% reduced incidence of all cause death. Most importantly, these beneficial effects were observed also in the elderly portion of the trial population, in striking contrast with the

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much higher blood pressure targets recommended as optimal by the recent hypertension guidelines [3,4].

Do the SPRINT results mean that guidelines should change their recommendations on blood pressure targets once again, this time reversing the previous conservative attitude and indicating the need to achieve a low blood pressure regardless patients' age? Clearly, the data made available by the press release do not allow a sufficiently informed opinion to be reached, for which we will have to wait publication of the full trial data, presumably in the next few months. It will be crucially important to know, for example, whether the benefit involved in a balanced fashion all cardiovascular outcomes or it was more pronounced on some rather than other cause-specific events. One candidate to a more pronounced benefit might be stroke which has been previously shown to decrease progressively with a treatment-induced reduction of blood pressure to lower values than cardiac events [10]. It will also be important to know whether lowering systolic blood pressure to 120 mmHg was associated with a substantial worsening of overall treatment tolerability, given that this happened in the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial on diabetic patients in whom reducing systolic blood pressure to about 119 mmHg was associated with a 3-fold increase of serious side effects compared to patients in whom systolic blood pressure remained above 130 mmHg [11]. This is a critical issue because in real life serious side effects often mean discontinuation of treatment which leads to a marked increase of cardiovascular risk [12,13], thus waning the expected benefit of treatment.

Publication of the SPRINT data will hopefully provide information on a third not less important question, for which its design may have an element of weakness, however. Namely, at which level of the blood pressure difference between the two groups is the greater benefit observed in patients with a lower blood pressure established. In other words, whether the greater cardiovascular protection occurred at a value only slightly less than 140 mmHg systolic blood pressure, around 130 mmHg or in the high or low 120 mmHg range. Further help in this direction will hopefully come from the European Society of Hypertension – Chinese Hypertension League Stroke in Hypertension Optimal Treatment (ESH-CHL SHOT) trial in which comparisons of the incidence of cardiovascular events at different target blood pressure is made between three rather than two groups [14]. This will allow to see whether different target blood pressure values exhibit a j curve rather than a straight line pattern, an observation that cannot be obtained when only two sets of data are available.

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