

Target blood pressure in high risk cardiovascular patients

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We appreciate the interest of Dreyfuss-Tubiana *et al.* (1) in the manuscript by Böhm *et al.* (2) investigating mean optimal blood pressure levels in the ONTARGET (3) and TRANSCEND (4) studies on cardiovascular events. We feel, however, that some points have to be addressed and clarified.

We agree that pulse pressure (PP) is of particular interest and associated with high risk for future strokes and cardiovascular mortality (5). However, therapeutic decisions are routinely based on blood pressure values, while PP is a calculated parameter of the difference between SBP and DBP and provides limited information about the actual extent of blood pressure values. PP can be identical in both hypertensive and normal or even hypotensive patients and can be confounded by vascular stiffness, aortic regurgitation. Furthermore, PP is hardly modifiable by treatment.

Markers predicting cardiovascular events

The authors argue that there is a need for additional markers identifying patients at risk for cardiovascular events. Collateral flow reserve has recently been shown to be decreased in patients with resistant hypertension considered for interventional treatment (6), indicating risk for coronary events. The risk for coronary artery disease as a result of long-lasting hypertension and classical risk factors might also indicate non-coronary atherosclerosis, with atherosclerosis being a systemic disease. Therefore, the carotid artery seems to be a valuable location which can be easily assessed non-invasively by doppler-

duplex ultrasound (7). However, regional differences of atherosclerotic lesions are highly prevalent and, therefore, this approach has limited sensitivity and specificity. Other biomarkers are associated with elevated blood pressure, such as the pro-inflammatory cytokine interleukin-6 as well as matrix metalloproteinase-9 and -2 (8). While cytokines and fibrosis markers have shown significant changes in hypertension, none of them have been scrutinized clinically relevant in terms of hard clinical outcome in large randomized controlled trials, nor is their routine assessment recommended by current guidelines. Therefore, further research is needed to investigate these biomarkers and their predictive value for clinical endpoints, they are impossible to explore in an outcome-trial on more than 30,000 patients (like ONTARGET/TRANSCEND).

New BP target defined by SPRINT?

ONTARGET investigated the effect of ACE inhibitors, angiotensin-receptor blockers or the combination on outcomes in high-risk patients with vascular disease or high-risk diabetes but without heart failure. The primary composite outcome was death from cardiovascular causes, myocardial infarction, stroke or hospitalization for heart failure (3). TRANSCEND recruited patients intolerant to ACE inhibitors, which received the angiotensin-receptor blocker telmisartan (4). Blood pressures in both studies were measured by health care professionals in the office (attended office blood pressure). Hence, the blood pressure values as measured in the SPRINT (9) trial can only be indirectly

compared to ONTARGET (3) or TRANSCEND (4), as to the vast majority of previous blood pressure trials, since SPRINT used a unique way of measuring unattended blood pressure with dedicated devices. A study comparing automated office blood pressure measurement, ambulatory blood pressure and office blood pressure has shown similar results for automated and ambulatory measurements as compared to falsely elevated attended office blood pressure measurements (10). This technique has been shown in previous studies to be comparable to or even lower than daytime ambulatory SBP, and thus up to 20 mmHg lower than the SBP values measured with the conventional attended measurement (10). This would translate blood pressure measurements in SPRINT to a BP goal of <140 mmHg in the intensive treatment group and approximately 155 mmHg in the standard treatment group, respectively (11), which is not different to previous studies. Therefore, the target SBP of 120 mmHg over 75 mmHg (DBP) indicates the pivot point of the J-curve and the underlying risk.

In conclusion, the J-curve indicates that blood pressure goals should take into consideration a lower boundary from where risk is increased, which is depending on the risk at baseline and can be different for different event types like stroke or myocardial infarction.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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