Stretching the carotid sinus to treat resistant hypertension

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Around a quarter of adults have hypertension, and by 2025, the number affected might be more than 1·5 billion people worldwide.[1] Despite important advances in pharmacotherapy in the past 40 years, resistant hypertension—that is, persistently raised ambulatory blood pressure despite treatment with at least three antihypertensive drugs, including a diuretic—occurs in about 13% of treated adults.[2] Optimisation of treatment is crucial in people with resistant hypertension because of the increased risk of cardiovascular disease. Two main pathophysiological mechanisms can be targeted: volume excess related to dietary sodium, reduced renal function, or aldosterone excess; and vascular resistance increased by overactivity of the renin–angiotensin–aldosterone system (RAAS) or sympathetic nervous system. Excess volume may be counterbalanced by use of high-dose diuretics or by adding a mineralocorticoid-receptor antagonist.[3] Vascular resistance may be reduced with RAAS blockers, β blockers, or interventional strategies. The baroreflex, which is controlled by the sympathetic nervous system, is mainly directed at short-term control of blood pressure. Several concepts have emerged suggesting that strong interactions between the sympathetic nervous system, the kidneys, and the RAAS contribute to long-term regulation of blood pressure.[4] Device therapies have been developed to target the sympathetic nervous system by baroreceptor stimulation or renal denervation.[5]

In *The Lancet*, Wilko Spiering and colleagues[6] present the CALM-FIM_EUR study, which is a first-in-human, proof-of-principle, open-label trial testing the safety and blood-pressure efficacy of a new interventional strategy to stimulate the endovascular baroreflex. The MobiusHD device (Vascular Dynamics, Mountain View, CA, USA) used in this study is a passive stent-like device that is implanted in the carotid artery to reshape the carotid sinus and reduce sympathetic outflow. 30 patients with baseline office blood pressure of 184/109 mm Hg and 24 h ambulatory blood pressure of 166/100 mm Hg underwent successful implantation. After 6 months, the values were significantly reduced by 24/12 mm Hg and 21/12 mm Hg, respectively. Five serious adverse events occurred in four patients (13%): hypotension, worsening hypertension, and intermittent claudication, each in one patient, and transient ischaemic attack in two patients.

This technique, based on a new concept, brings hope through a simple and efficient interventional strategy. However, similar blood-pressure drops were previously achieved with renal denervation or second-generation baroreceptor activation therapy in open-label studies,[7,8] but the effects were overestimated due to several confounders, such as the placebo effect, the Hawthorne effect, or treatment adherence. Assessments in randomised studies, therefore, were disappointing, with either no or limited blood-pressure benefits being seen. Although the authors included measurements of ambulatory blood pressure, which theoretically limits the placebo effect, the true blood-pressure benefit with the MobiusHD device, if any, might be lower than in the initial findings.

The main objective of the study was safety, and the profile is presented as acceptable compared with that for more invasive techniques. This statement, however, should be interpreted with caution owing to the two transient ischaemic attacks encountered. The risk-to-benefit balance needs to be more precisely assessed. The long-term efficacy of passive reshaping of the carotid is unclear because of the known dynamic physiology of the baroceptor reflex and the classic resetting phenomenon and possible late neoatherosclerosis around the MobiusHD device. Finally, Spiering and colleagues did

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not directly measure adherence to medication in blood or urine,[6] but this method would have considerably strengthened the validity of the study.

The experience from previous device trials of renal denervation and baroreceptor activation therapy in patients with resistant hypertension underscores the relevance of sham controls[9–11] and direct measurement of adherence to medication.[12] Consequently, a study that includes a sham intervention, a standardised antihypertensive treatment, and direct measurement of medication adherence is highly warranted before any conclusions can be drawn about the MobiusHD device. While waiting for these trials, the CALM-FIM_EUR is an important hypothesis-generating study in the difficult field of resistant hypertension. If a blood-pressure benefit is confirmed, this device will certainly strengthen the array of devices available for improving blood-pressure control.

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