

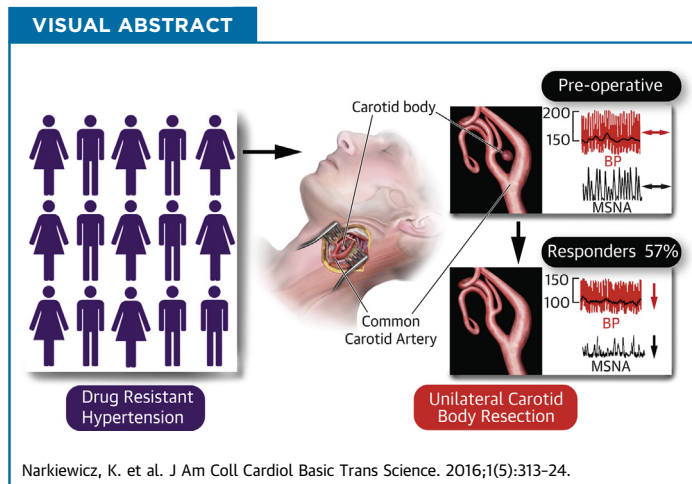
## CLINICAL RESEARCH

# Unilateral Carotid Body Resection in Resistant Hypertension



## A Safety and Feasibility Trial

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## HIGHLIGHTS

- First prospective feasibility and safety clinical trial on unilateral CB resection for the treatment of high blood pressure.
- In drug-resistant patients with hypertension, unilateral CB resection was feasible and safe.
- Unilateral CB resection lowered blood pressure by 26 mm Hg in 57% of patients with drug-resistant hypertension associated with a reduction in muscle sympathetic nerve activity and its baroreceptor reflex control.
- Whole drug equivalents were reduced in the responding patients.
- Responding patients had characteristics distinct to those that did not respond; these should allow patient selection for future CB modulation trials.

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**ABBREVIATIONS  
AND ACRONYMS****ABP** = ambulatory blood pressure**ASBP** = ambulatory systolic blood pressure**BRS** = baroreceptor reflex sensitivity**CB** = carotid body**HRV** = heart rate variability**HVR** = hypoxic ventilatory response**MSNA** = muscle sympathetic nerve activity**OBP** = office blood pressure**OSBP** = office systolic blood pressure**uCB** = unilateral carotid body**SUMMARY**

Animal and human data indicate pathological afferent signaling emanating from the carotid body that drives sympathetically mediated elevations in blood pressure in conditions of hypertension. This first-in-man, proof-of-principle study tested the safety and feasibility of unilateral carotid body resection in 15 patients with drug-resistant hypertension. The procedure proved to be safe and feasible. Overall, no change in blood pressure was found. However, 8 patients showed significant reductions in ambulatory blood pressure coinciding with decreases in sympathetic activity. The carotid body may be a novel target for treating an identifiable subpopulation of humans with hypertension. (J Am Coll Cardiol Basic Trans Science 2016;1:313–24) © 2016 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

**F**ound bilaterally at the bifurcation of the common carotid artery, the carotid bodies (CBs) are strategically located to ensure that adequate oxygen is supplied to the brain. With the highest blood flow per tissue weight of any organ (1), they are exquisitely sensitive to small alterations in blood oxygen, carbon dioxide, pH, and blood flow itself (2,3). Despite their small size, the CBs exert powerful reflex effects on the respiratory and cardiovascular system (4) that have been preserved through evolution and are deemed pivotal for survival (5), perhaps due to their defensive reflex role. This powerful afferent system normally remains quiescent at sea level in resting conditions, but during hypoxia, the CBs are activated, increasing ventilation, increasing sympathetic activity, inducing alkalosis, and contributing to periodic breathing during sleep (6,7).

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In patients with hypertension, the CBs exhibit both hyper-reflexia and aberrant discharge; in sleep apnea, the activation of the CBs is, in part, responsible for the excessive sympathetic activity and hypertension associated with this condition (8). Moreover, the hypertension evoked in a rat model of sleep apnea (by chronic intermittent hypoxia), is reliant on afferent activity generated by the CBs (9), and patients with hypertension may have exaggerated peripheral chemoreflex sensitivity to hypoxia (10,11). Additionally,

acute reversible inactivation of the CBs, with hyperoxia, caused a transient reduction in blood pressure (BP) and muscle sympathetic nerve activity (MSNA) in patients with hypertension (12). In rats with hypertension, severing the connection between the CBs and brain lowered both arterial pressure and sympathetic activity chronically (13). These data point toward the CBs as a therapeutic target to treat sympathetically mediated diseases (14). The global clinical problem and financial burden of hypertension continues to escalate (15), and 8% to 14% of the 1 billion patients with hypertension worldwide are drug resistant or intolerant (16). Therefore, new approaches for treating drug-resistant hypertension are justified, as are studies to identify the targets/mechanisms driving hypertension. We describe the first prospective proof-of-concept, safety and feasibility study of unilateral (u) CB excision from a cohort of patients with drug-resistant hypertension. We report, secondarily, on the proportion of these patients that showed a response in BP, the hypoxic ventilatory response (HVR), and MSNA.

**METHODS**

**STUDY DESIGN AND PATIENTS.** We present pooled results from 2 independent centers in which the primary endpoints were safety and feasibility of uCB excision in patients with drug-resistant hypertension. Secondary endpoints were to assess the proportion of

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