Reply

Yusuke Sata[a,d], Geoffrey A. Head[b], Murray D. Esler[a,c], and Markus P. Schlaich[a,c,d,e]

We thank Okon *et al.* [1] for their interest in our recently published findings related to the utility of ambulatory arterial stiffness index (AASI) in predicting the response to renal denervation (RDN) in patients with resistant hypertension [2]. Sympathetic excitation is a hallmark of essential hypertension [3,4] and is further exaggerated in patients with resistant hypertension [5], findings that provided the fundamental basis for the introduction of catheter-based RDN to clinical medicine [5]. The pathophysiology of resistant hypertension is undoubtedly multifactorial and aside from sympathetic overdrive, impaired volume homeostasis and arterial remodelling, amongst others, are key factors that may contribute to the scenario. The contribution of each of these important factors is likely to vary substantially between affected individuals rendering a 'one-fits-all' therapeutic approach problematic. Indeed, an important lesson from previous RDN studies was that the blood pressure (BP) response to the procedure varies substantially between individuals. Efforts to better understand this variability revealed that arterial stiffness or surrogate markers thereof, as assessed by a number of complementary techniques including pulse wave velocity (PWV) [6], isolated systolic hypertension and pulse pressure (PP) [7], augmentation index [8] and others, appear to be relevant modulators of the BP response to RDN.

Our recent findings in patients with resistant hypertension extend our knowledge to yet another marker of arterial stiffness, namely AASI [1]. In line with other reports [6–8], patients with an AASI below the median had a more pronounced BP response to RDN, supporting the validity of the conceptual framework within which patients with stiffer arteries and therefore a predominant structural component underlying their treatment resistance are less likely to respond to an intervention targeting primarily sympathetic overactivity. Indeed, patients in the highest AASI quartile had the lowest level of muscle sympathetic nerve activity [2]. Of note and in contrast to the statement by Okon *et al.* [1] in their letter, we clearly do not consider AASI as a valuable marker of sympathetic activity. They question the utility of AASI as a marker of arterial stiffness and raise some valid points regarding the limitations of various markers of arterial stiffness and that these are not interchangeable but reflect different aspects of the continuous process of vascular remodelling, which we agree with. Similarly, we agree that PWV remains the gold standard in assessing arterial stiffness, although its utility is limited in a number of settings including atrial fibrillation, peripheral and carotid artery disease, obesity and left ventricular dysfunction including aortic stenosis, which are not infrequently encountered in patients with resistant hypertension and elderly.

In the context however, practicability and accessibility to relevant techniques for more wide-spread clinical use to assess the likelihood of a significant BP response to RDN is an important factor. Devices to assess PWV are not commonly available outside an academic research setting, are costly and their use requires trained personnel. AASI in contrast can easily be derived from 24-h ambulatory BP recordings accessible to most clinicians dealing with hypertensive patients by simple calculations. Although AASI is a relatively newly established marker, it has clearly been shown to predict cardiovascular outcomes. In the Dublin Outcome Study including 11 291 patients with a median of 5.3 years of follow up, AASI was a better predictor than PP for stroke and independently predicted cardiovascular mortality, even in normotensive individuals [9]. Similarly, In a Japanese population, AASI predicted cardiovascular and stroke mortality over and beyond PP and other risk factors [10]. Although acknowledging the limitations of AASI and the uncertainty of the exact aspect of vascular remodelling AASI may best reflect, these data in our view support the use of AASI as a simple and practical approach to assist in the decision-making of whether or not RDN may be a therapeutic approach to be considered in patients with resistant hypertension. Further prospective studies would be most useful to determine which markers are superior in predicting the BP response to RDN.

Finally, Okon *et al.* are puzzled by the finding of a reduction in AASI after RDN in the highest AASI quartile, that is in those patients with the least favourable BP effects. We hypothesize that although the immediate BP response may be diminished in these patients due to substantial vascular remodelling, longer term beneficial effects of sustained reduction in sympathetic drive [11] even in the presence of potential anatomic reinnervation [12], may render RDN useful in those with stiffer arteries. This however, will have to be investigated in longer term follow-up studies.

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Conflicts of interest

There are no conflicts of interest.

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[a]Neurovascular Hypertension and Kidney Disease Laboratory, [b]Neuropharmacology Laboratory, Baker Heart and Diabetes Institute, [c]Department of Cardiovascular Medicine, Alfred Hospital, [d]Faculty of Medicine, Nursing and Health Sciences, Monash University, Melbourne, Victoria and [e]Royal Perth Hospital Unit, Dobney Hypertension Centre, School of Medicine, University of Western Australia, Perth, Western Australia, Australia

Correspondence to Markus P. Schlaich, Dobney Chair in Clinical Research School of Medicine, Royal Perth Hospital Unit, The University of Western Australia, Level 3, MRF Building, Rear 50 Murray St, Perth 6000, WA, Australia. Tel: +61 8 9224 0334; e-mail: markus.schlaich@uwa.edu.au

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