The recent introduction of renal denervation therapy for hypertension has drawn much attention to the problem of resistant hypertension. The frequent failure of medical therapy, as well as expectations that a new era of device-based treatment may be beginning, has encouraged research in this area. It is in this context that Diaz et al1 provide new data on the association of apparent treatment-resistant hypertension (aTRH) with patient characteristics, as well as outcome (cardiovascular events, all-cause mortality, and cardiovascular mortality), in the population-based REasons for Geographic And Racial Differences in Stroke (REGARDS) study.

It is important to realize that aTRH is not a pathophysiologic entity. It is frequently thought to be associated with secondary hypertension. If this is indeed the case, the pathophysiology of aTRH stems from widely diverse mechanisms: an increase in sympathetic nervous system dysregulation related to obstructive sleep apnea, renin–angiotensin activation, volume excess (be it dietary, caused by renal dysfunction or hyperaldosteronism), use of exogenous agents (birth control pills, alcohol, licorice), etc. The expectation that such a vast array of pathophysiologic mechanisms can be solved by a focused intervention, such as renal denervation, was not fulfilled when studied meticulously.2

Most guidelines stress the importance of both noncompliance with medical therapy and volume excess as major causes of aTRH. A recent study found absence of the prescribed medications from the urine in at least half the patients diagnosed with aTRH.3 Volume excess may stem from excess salt consumption, and the association of obesity with aTRH is common. In our salt-laden society, obese people consume a larger amount of food than leaner ones, relative to their energy expenditure, consuming more salt. Therefore, volume excess, like medication noncompliance, may also be regarded as a behavioral pattern.

Physicians tend to blame treatment failures on their patients. However, if physicians do not explicitly review their patients dietary, lifestyle, and medication recommendations, patients’ compliance is likely to be limited. Additionally, it is we physicians who are to blame for therapeutic inertia when facing aTRH4 and our frequent noncompliance with hypertension guidelines. Noncompliance with guidelines also leads to the common failure to refer patients with aTRH to physicians experienced with treating aTRH. Therefore, I think aTRH is not only related to noncompliance of patients, but also of physicians.

The study of aTRH in the REGARDS population examines the association of 6 healthy lifestyle factors (HLSFs) to outcome in this population: moderate alcohol consumption, physical activity, and current smoking by telephone questions, waist circumference by actual home visit measurement, and Dietary Approach to Stop Hypertension (DASH) diet score and ratio of sodium to potassium intake from a self-administered food frequency questionnaire.

About two thirds of participants had none or at most 2 HLSFs. Only 13% had ≥4 HLSFs. For this reason, Diaz et al1 considered those with ≥4 HLSFs as 1 group to obtain a large enough group for a meaningful analysis. The prevalence of aTRH, 14%, was similar to other aTRH cohorts. The low prevalence of ≥4 HLSFs is not surprising: in the National Health and Nutrition Examination Survey (NHANES) 2001 to 2006 among people diagnosed with hypertension, prevalence of ≥4 HLSFs was ≈20% and ≈5%, respectively,7 and in rural Minnesota, only 1% of participants of a survey had an ideal lifestyle according to the American Heart Association lifestyle guidelines.6

Obesity carries a notoriously high prevalence of uncontrolled hypertension, despite more intensive therapy,7 and the commonly associated metabolic syndrome is associated with dyslipidemia, physical inactivity, and hyperinsulinemia. Because many of these risk factors are related, it is not surprising that the hazard ratios of events associated with the cumulative number of HLSFs do not change in direction despite the extensive adjustment for different characteristics and risk factors. This suggests that they have little additive effect when combined. However, not all HLSFs had similar protective effects in this aTRH cohort. Only nonsmoking and physical activity had a robust protective effect. High DASH diet score had an isolated effect on all-cause mortality, whereas the Na/K ratio was not predictive. It is important to note that the Na/K ratio was inferred from a questionnaire and does not necessarily accurately reflect sodium intake.8,9 Interestingly, absence of abdominal obesity (defined by waist circumference) was associated with increased unadjusted hazard ratios for cardiovascular events and all-cause mortality. The hazard ratios lost significance when adjusted but remained with a trend for increased risk.

See related article, pp 465–471

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Hypertension is available at http://hyper.ahajournals.org
DOI: 10.1161/HYPERTENSIONAHA.114.03687

Editorial Commentary

Resistant Hypertension and Healthy Lifestyle
Impact on Prognosis

Michael Bursztyn
Previous studies have also demonstrated a higher risk in lean hypertensives. This may be attributable to an association with smoking and higher alcohol intake, consistent with attenuation of the hazards ratio after adjustment for these factors in the aTRH REGARDS study. The interaction of lean hypertension with an increased likelihood of an adverse outcome was recently confirmed in a large meta-analysis, although the association was of marginal clinical importance.

Abdominal obesity is an example of the complexity of competing risk factors on outcome. Although the associations found by Diaz et al do prove the relationship of the HLSFs with event-free survival, recommending HLSF as therapy can only be proven in a meticulous intervention study, which is not likely to materialize. Meanwhile, we should use cautious common sense in translating the suggestions of the study by Diaz et al to clinical practice. Given the low and decreasing prevalence of HLSFs, we cannot be optimistic that a healthy lifestyle will have a significant impact on aTRH prognosis.

Disclosures

None.

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Hypertension. 2014;64:459-460; originally published online June 9, 2014;
doi: 10.1161/HYPERTENSIONAHA.114.03687

Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2014 American Heart Association, Inc. All rights reserved.
Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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