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NEW INVESTIGATOR PAPER

Refractory hypertension: A new phenotype?

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Refractory hypertension is not a continuum of resistance to blood pressure treatment, but a new phenotype that demands anticipation and priority. In fact, we are talking about two sides of the same disease.

Refractory hypertension was recently described, and its definition is still being developed.¹ Initially, it was described as an extreme phenotype of resistant hypertension – a continuum of severity – based on the premise that the evolution of hypertension is a cycle in which high blood pressure (BP) causes more endothelial dysfunction and consequently a higher increase in BP, that is, higher resistance to treatment. Currently defined as uncontrolled BP despite the use of 5 or more drugs, including a long-acting thiazide diuretic and a mineralocorticoid receptor antagonist, refractoriness deserves to be better discussed and investigated.^{2,3}

For over 20 years, I have been following a large cohort of resistant hypertensives and it was possible back then to distinguish a more severe clinical presentation, frequently associated to younger patients. That situation did not seem to be related to a progressive worsening of a disease caused by endothelial dysfunction since it was less prevalent in individuals with resistant hypertension for many years. Actually, it was noticed mainly in those ones with hypertension of early beginning.

From this initial definition, several studies were developed analyzing the pathophysiology of refractory hypertension and it looks better elucidated nowadays. These findings point out that sympathetic hyperactivity is related to refractoriness while resistant hypertension would be more associated to volume component and hyperaldosteronism status with a good response to diuretics and mineralocorticoid receptor

antagonists, reinforcing the hypothesis that these are two distinct clinical conditions.^{2,3}

Another point that still needs to be better defined is whether refractoriness should be based on the absence of office BP control or ABPM/HBPM. Since ABPM is mandatory in resistant hypertension clinical follow-up, I believe that refractory hypertension should also be based on uncontrolled out of office BP without the need of using the distinctive term true refractory hypertension.⁴

In different populations described so far, refractory patients are more frequently women, younger, obese, diabetic and have metabolic syndrome.^{5,6} Most of the studies have described a high prevalence of asymptomatic hypertension-mediated organ damage.^{3,5} Being a historical cohort, in our recently published study⁶ we were able to divide refractory patients between pre- and post-spirolactone eras. Surprisingly, we identified that, despite the lack of BP control when using 5 or more drugs, the introduction of spironolactone showed an improvement in the cardiovascular risk profile with less aortic stiffness and decrease in left ventricular mass. Still, further robust longitudinal studies are needed to let us know the actual prognosis of refractory hypertension.

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NEW BLOOD

Mentoring: a priceless relationship

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Priceless. Crucial. Helpful. Opportunity. Network. Satisfying. These were the words the six senior members of our research community used to describe their mentoring experience when interviewed for the [ISH Podcast](#) in 2020. Professor Rhian Touyz, the first female president of the ISH as well as the first mentor we interviewed, said “Mentorship is important because I feel one can always learn from others”. Professor Stephen Harrap, also a past ISH president, spoke about mentoring

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providing “an objective independent view to the mentee”. Professor Maciej Tomaszewski, current president of the ISH, adds “You need someone who you can look up to because that makes your life much easier and you can benefit enormously”.

It was inspiring to hear the many ways our interviewees have helped their mentees. Examples included guiding them on career choices after training or how to climb the professional ladder,