LEARNING THE ROPES

A Primer on Secondary Hypertension

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In its “Global Hypertension Practice Guidelines”, released earlier this year, the **International Society of Hypertension** noted that “Early diagnosis of secondary hypertension and the institution of appropriate targeted treatment have the potential to cure hypertension in some patients or improve BP control/reduce the number of prescribed antihypertensive medications in others.” Despite such attention, it is generally agreed that secondary hypertension remains underdiagnosed. In this “Learning the Ropes” feature we discuss, at length, secondary hypertension. You will find in-depth features on the various causes of secondary hypertension from three world experts.

It has been about 80 years since Goldblatt established the concept of renal artery stenosis causing hypertension¹. At the time of his seminal observations, and in the absence of blood pressure lowering drugs, surgical interventions such as aortorenal, splenorenal, and hepatorrenal bypasses represented the only therapeutic options. By 2020 though, surgical interventions have been virtually replaced by renal angioplasties with stents. More importantly, several classes of blood pressure lowering drugs, developed over the past decades, provide an impressive armamentarium to treat the consequence of renal artery narrowing, that is lower the high blood pressure, and thereby avert the adverse consequences associated with high blood pressure. Furthermore, the ever-expanding knowledge of natural history of atherosclerotic plaque formation and stability together with the development of lipid lowering drugs such as statins and antiplatelet agents allows for comprehensive pharmacotherapy of atherosclerotic renal artery stenosis beyond blood pressure control *per se*. As Prof. Markus Schlaich elegantly points out in our first feature “**Atherosclerotic Renal Artery Stenosis**”, there appears to be an absence of evidence favouring angioplasty and stenting as compared to comprehensive pharmacotherapy of atherosclerotic renal artery stenosis associated hypertension. He points out though, that a significant gap in the evidence for management of patients with atherosclerotic renal artery stenosis caused hypertension remains, as patients with truly resistant hypertension, progressive renal function loss, and recurrent acute heart failure (in the absence of underlying ischemic or structural heart disease) associated with rapid and severe increase in blood pressure (flash pulmonary edema) were either excluded or underrepresented in the published

trial literature. Until such evidence becomes available, at least for these patients, renal angioplasty with stenting could and should be considered at experienced centres.

In our second feature, Prof. Maria-Christina Zennaro highlights the most common form of secondary hypertension, **“Primary Aldosteronism”**. Well highlighted is the fact that early detection and treatment is crucial as primary aldosteronism carries a disproportionately higher risk for subsequent cardiovascular complications compared with essential hypertension.² Importantly, much of the excess cardiovascular risk in primary aldosteronism occurs independent of blood pressure. While historically considered a rare condition, recent studies have highlighted the high prevalence of primary aldosteronism which remains vastly underappreciated with a large number of cases still undiagnosed.^{3,4} Beyond the under-diagnosis of primary aldosteronism as defined by conventional clinical criteria, there is a growing appreciation for the existence of a continuum of renin-independent aldosteronism and excess mineralocorticoid receptor activation beyond these criteria that may contribute to a large portion of what we currently label as “essential hypertension”. Over the coming years, we are likely to witness a transformation in our understanding of the true spectrum of primary aldosteronism that will allow for earlier identification and novel targeted therapeutic approaches for a much broader population aimed at cardiovascular disease prevention.

In the shadow of primary hyperaldosteronism and atherosclerotic renal artery stenosis remain other rare forms of hypertension. Adrenal gland pathologies range from tumor-related excessive production of hormones intimately involved in the regulation of circulatory homeostasis to the imbalance between hormones normally produced because of enzymatic defects. As Prof. Peter de Leeuw elegantly points out in our final feature **“Other Endocrine Causes of Hypertension”**, these forms of hypertension are rare, diagnosis is fairly complex and resource intensive, and more likely than not will require an involvement of a specialist. The same could be said about hypertension associated with hyperparathyroidism or acromegaly. As Prof Peter de Leeuw highlighted, systolic hypertension associated with hyperthyroidism is more a secondary rather than primary feature of the disease, though if missed and left untreated could lead to high output heart failure. Similarly, as for other forms of hypertension, diagnosis of these rare forms is crucial, as targeted/specific treatments are frequently available and curative. A missed diagnosis may, on the other hand, leave patients with these rare forms of hypertension labelled with “hypertension resistant to pharmacotherapy”.

References:

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