Primary aldosteronism (PA) may be the best treatable risk factor for cardiovascular disease besides to quit smoking. The discovery of the disease is described in Prof. Gordon’s chapter in this book, and the understanding of its prevalence and the epidemiology behind it as well. Thus, PA is common, and millions and millions of individuals worldwide most likely suffer from undiagnosed PA as an underlying reason for their hypertension. To improve the diagnose of PA, understand the derangements and what consequence untreated PA lead to is crucial for development of care of individuals with PA.

Consequences of PA are bearing the risk factor not only for cardiovascular disease but also on life quality. Drs. Stowasser and Ahmed describe the important QoL assessments that have been done until now in one section of this book. It is clear that improvement of QoL is the effect of medical as well as surgical treatment, with a more rapid effect after surgical treatment. Besides the positive effects seen by the reduced blood pressure per se, also less need of medication with reduced negative side-effects with benefits surgery. Reversal of PA also leads to positive effects on various psychological measures, caused by so far unknown mechanisms. Aldosterone is a risk factor for cardiovascular disease, which may be reduced by proper treatment of PA. Thus, there is a higher incidence of cardiovascular events in PA-associated hypertension than in age- and sex-matched populations with essential hypertension.

The diagnostic procedures for PA are discussed in several chapters in this book, commenting on the aldosterone–renin ratio (ARR), confirmatory testings, and the adrenal venous sampling. In clear cases the diagnosis is easy, but in the majority these methods may certainly be beyond the sensitivity level. Thus, a major issue is identification and treatment of early or “subclinical” PA, among patients with essential hypertension. Indeed, there seems to be a continuum of this disease into the entity denoted low-renin hypertension, which in many cases is a mild form of early or subclinical PA. Indices state that this form of the disease is also associated with increased risk for cardiovascular complications and possibly reduced QoL. Today, the method of choice to identify PA is the aldosterone/renin ratio, which has been
used also for screening of populations with essential hypertension. However, this method has a number of drawbacks as being sensitive for ongoing medications, posture, diet, etc. In addition, assays of aldosterone and, especially, renin have been unsensitive. Although the ARR still is the most available method to possibly identify also early PA, a continuous search for alternative diagnostic methods to increase the possibility to identify also early “subclinical” PA is needed.

If performing the ARR is a problem, also the confirmatory testings are sometimes difficult with far less than 100% sensitivity and specificity. Moreover, lateralization may be determined by adrenal venous sampling, but it also has its well-known technical difficulties. Recent development in using positron emission tomography (PET) by, for instance, $^{11}$C-metomidate as tracer after Dexamethasone suppression is promising in distinguishing aldosterone-producing from hormonally inactive adenomas.

The recent developments in understanding the genetics behind sporadic PA may lead to novel methods to diagnose the disease in the future. Although no success has been described yet in identifying, for instance, mutated KCNJ5 in plasma samples, further investigations are needed. The identification of mutations in KCNJ5, ATP1A, ATP2B3, and CACNA1D has also made understanding of the pathophysiology of the zona glomerulosa cells more clear. The importance of the membrane potential and depolarization for release of aldosterone is obvious.

Treatment of PA is either medical or surgical. The medical treatment of PA is limited to spironolactone and eplerenone, where the latter has considerably less side effects. This is recommended especially in idiopathic hyperaldosteronism (IHA) where surgery has limited effect due to its bilateral cause. However, in certain cases with asymmetrical nodular hyperplasia, a unilateral adrenalectomy may still be beneficial. Interestingly, Dr. Takeda and coworkers comment on the possible epigenetic factors influencing the disease, by proposing that the methylation of CpG islands in the CYP11B2 promoter region may regulate the activity of transcription of this gene, and consequently the amount of aldosterone produced and the level of PA. Long-term treatment with, for instance, spironolactone has in some cases induced, or being associated with, remission of the PA, possibly due to a changed methylation status.

While medical treatment in cases with IHA or milder forms may be successful, surgical treatment has an excellent outcome, and today the laparo- or retroperitoneoscopic approach is an easy procedure for the patient who may leave the hospital the following day. Reversal of PA is instant after surgery, with a dramatic reduction of the number of hypertensive drugs and no need for potassium supplementation, as well as improved QOL and reduction of risk for cardiovascular complications.

The present book presents the disease of primary aldosteronism from pathophysiology to quality-of-life aspects, covering genetics, diagnostics, and different treatments in a truly translational manner.

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