

## *Strategies to interfere with progression of renal disease*

Eberhard Ritz  
Ruperto Carola University  
Heidelberg (Germany)

The prevalence of chronic kidney disease has recently increased dramatically throughout the Western world, primarily because of the increasing prevalence of the metabolic syndrome and of type-2 diabetes.

It is important that not all patients with chronic kidney disease (CKD) progress to renal disease. Indeed, the risk to die from cardiovascular causes is greater than the risk to reach endstage renal disease (ESRD).

There is consensus that the two most important therapeutic approaches to prevent progression are *treatment of high blood pressure* (particularly systolic BP) and of *proteinuria*.

Blood pressure should be lowered to values less than 130 mmHg and that this should be accompanied by blockade of the renin angiotensin system. In addition, however, proteinuria should be reduced to levels less than 1000 mg/24 h and potentially even less.

To achieve these goals it is usually necessary to combine four or more antihypertensive agents. A neglected aspect is reduction of salt intake and treatment with diuretics.

In order to reduce proteinuria it is often necessary to use ACE-inhibitors or angiotensin receptor blockers in doses higher than those licensed for lowering blood pressure.

The role of mineralocorticoid receptor blockade is currently unclear because important safety issues (hyperkalemia) have not yet been resolved.

In addition to these mainstays of treatment, a number of important but often neglected aspects of treatment deserve consideration.

*Cigarette smoking* increases dramatically the risk of onset and of progression of CKD. There is observational evidence that cessation of smoking retards progression.

*Obesity* is also an important risk factor for the onset and progression of CKD. Uncontrolled interventional studies clearly document that reduction of obesity attenuates progression, although this intervention should no longer be considered in advanced CKD, because then weight loss aggravates the cardiovascular risk.

Particularly in the elderly with CKD, use of *non-steroidal anti-inflammatory agents* is common and this has been shown to accelerate renal function loss.

In diabetic patients *glycemic control* is of overriding importance particularly in the initial stages, yet it makes a relatively less important contribution to progression once renal function is impaired. Adequate glycemic control is nevertheless of great relevance to reduce the microvascular and macrovascular risks.

In diabetic patients the importance of combining interventions (multifactorial intervention) has been clearly demonstrated and this will have consequences for the management of nondiabetic patients with renal disease as well.

For several interventions the formal evidence that progression is attenuated has not yet been provided in humans, but which appear to be sensible based on observational or animal data, e.g. correction of anemia, administration of active vitamin D and others.