The Kidney
Both Culprit and Victim
Eberhard Ritz

Today, it is universally acknowledged that, in hypertension, the kidney is both culprit and victim. Kidney malfunction causes hypertension, and hypertension, in turn, aggravates chronic kidney disease (CKD) and accelerates its progression. High blood pressure (frank hypertension and blood pressure values in the high normal range) are clearly correlated to progressive kidney injury, both in experimental
and in clinical observations. All of the current guidelines recommend lowering of systolic blood pressure to 130 or 125 mm Hg in CKD, and even lower values are recommended if the target level of proteinuria of <1 g per 24 hours has not been achieved. There is good evidence of “renoprotection” by lowering blood pressure in patients with renal disease, at least in the presence of proteinuria. In CKD patients without proteinuria, eg, autosomal polycystic kidney disease, further renoprotection cannot be achieved by lowering blood pressure below the target blood pressure recommended in patients without CKD; nevertheless, these patients have a markedly elevated cardiovascular risk, and more stringent lowering of blood pressure is desirable, because, eg, reduction of left ventricular hypertrophy as an index of cardiovascular risk had been documented in such patients.

The worldwide problem of neglect of hypertension and of insufficient implementation of antihypertensive treatment in CKD patients prompted the International Society of Nephrology and the International Federation of Kidney Foundations to devote this year’s World Kidney Day (http://www.worldkidneyday.org) on March 12th to the issue of hypertension.

Disappointingly, the assessment of blood pressure in patients with CKD almost uniformly shows a high frequency of uncontrolled blood pressure. To take one example, in the recent Kidney Early Evaluation Program, a reasonable prevalence of awareness (80.2%) and treatment (70.2%) contrasted with a miserable control rate of blood pressure (13.2%), mostly of systolic blood pressure. This topic is confirmed and extended by the present analysis by Platinga et al (in this issue) based on the data of the National Health and Nutrition Examination Survey 1999–2006. The report provides good news and bad news. The good news is that there is a trend for improvement of blood pressure control in general. The bad news is that this is less pronounced and not statistically significant in patients with CKD stages 3 and 4. The study identifies major deficits in the type of treatment, as described below.

The first deficit is an insufficient number of hypertensive medications (≥2 classes of drugs in only 25% of CKD patients, whereas in my experience, to achieve blood pressure targets in CKD patients, the administration of ≥4 antihypertensive medications is more the rule than the exception. Second, Platinga et al found surprisingly infrequent use of angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers (in only 24.2% of CKD patients!). Finally, even more surprising in the current era of high dietary salt intake, the researchers identified insufficient use of diuretics (only 18.5% in CKD patients!).

The study has several limitations. Office blood pressure (although the only practical approach in such a huge, population-based study) is the least reliable predictor of cardiovascular and presumably also renal risk compared with home blood pressure (self-measurement) or ambulatory blood pressure. This is particularly true in the renal patient where nocturnal blood pressure tends to be disproportionally elevated and central blood pressure disproportionately higher than peripheral blood pressure. Second, the analysis is based on blood pressure measurements at a single point in time, which again reduces the accuracy of the estimate of the blood pressure burden to target organs. We are not given detailed information on patient nonadherence, which is one (certainly not the only) reason for poor blood pressure control.

The authors wisely restricted the analysis to patients with CKD stages 3 and 4. However, as recently pointed out by several authors, CKD stage 3 is almost certainly composed of 2 different states, ie, with and without urinary abnormalities: patients with proteinuria have substantially higher cardiovascular and renal risks. Better distinctions of these subtypes will be a task for future studies.

The almost uniformly poor control of hypertension in CKD patients worldwide raises the issue of how this can best be corrected. There is no simple answer, and certainly both physicians and patients must be targets for efforts to improve this dismal situation.

It has been shown that many physicians do not know the risk factors leading to hypertension, neglect the recommended target blood pressure, fail to use combination therapy with multiple antihypertensive agents, and also succumb to the misconception that the renin-angiotensin system blockade settles the issue, a “fire-and-forget” mentality. With respect to diuretics, many physicians do not appreciate that proteinuria alters the pharmacokinetics: diuretics act on tubular sodium transporters from within the tubular lumen, but it is only the nonprotein-bound fraction that is effective as an inhibitor of
sodium transport. In the presence of heavy proteinuria, higher doses have to be used. Because thiazide monotherapy is no longer fully effective at serum-creatinine concentrations above \(\approx 3 \text{ mg/dL}\), furosemide has to be used. In view of its short effective half-life, the common once-per-day administration is suboptimal. In short, one road to improve matters is to educate physicians. On the other hand, other barriers to overcome are deficits on the patient side, including frequent lack of knowledge of the link between blood pressure and poor renal outcome, noncompliance, and incomplete appreciation of the enormous cardiovascular risk associated with CKD. Better patient education and raising patient awareness are certainly important goals. One of the best instruments to create awareness and a more positive attitude to blood pressure control is self-measurement of blood pressure. This has the additional advantage of being superior to office blood pressure measurements as a predictor of renal and cardiovascular risk.

Finally, on a population level, the issue of reducing dietary salt intake both in nonrenal patients, but particularly in renal patients, has to be addressed. Although controlled, prospective evidence is painfully absent, relatively short-term data in renal damage models of rodents and long-term studies in chimpanzees, as well as acute interventions in patients with CKD, provide a strong argument for reduced salt intake in CKD. The ability of the patient to limit his or her dietary intake is limited, because only 15% to 20% of dietary salt is under the direct control of the patient, and 85% is already contained in commercial food items. Interventions in Finland and in the United Kingdom have shown that a population-based approach to tackle this problem is both effective and doable.

The present study by Platinga et al.\(^9\) has the merit to, again, have focused attention on deficits in blood pressure control of renal patients. Given the frequency of this condition and the devastating impact of high blood pressure on the development of renal failure, blood pressure control deserves heightened attention, not just because end-stage kidney disease poses an enormous cost burden to the health system and dramatically reduces the quality of life. Blood pressure control is the most effective intervention to retard or prevent end-stage renal disease and its cardiovascular complications.

Disclosures
E.R. is a past member of the advisory board for Boehringer and a Steering Committee member of ROADMAP Trial (Daichi Sankyo).

References
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