Controlling BP Is Critical for People With CKD

Written by Mary Beth Nierengarten

In a session at the Joint Meeting of the European Society of Hypertension and International Society of Hypertension on hypertension in chronic kidney disease (CKD), a panel of experts discussed the critical need to control blood pressure (BP) for patients with CKD, issues in diagnosis and management, and specific issues in patients with end-stage renal disease (ESRD).

CHANGING EPIDEMIOLOGY OF CKD: INCREASING NUMBER OF PEOPLE WITH UNCONTROLLED BP AT RISK OF DEVELOPING CKD AND ESRD

Roland E. Schmieder, MD, Professor of Internal Medicine, Nephrology, and Hypertension, University Hospital Erlangen, Erlangen, Germany, opened the session with an overview of the changing epidemiology of CKD in the general population. He highlighted that hypertension and diabetes are the major contributors to the increasing prevalence of CKD, causing up to 60% of cases of CKD in 2014. Hypertension is the primary contributor to progressive disease, he said, indicating that better BP control is critical to slowing down the increasing incidence of ESRD. Data from the Framingham Offspring study showed that the lifetime risk of developing ESRD in the general population was 9.4% [Drev N et al. *Am J Kidney Dis* 2003] and that the incidence increased with advancing age, diabetes, hypertension, smoking, obesity, and a lower baseline glomerular filtration rate (GFR).

To reduce the incidence of ESRD and to better manage patients with CKD, patients who are at high risk of developing renal and cardiovascular disease need to be identified. Two tools—estimated GFR (eGFR) and urine albumin-to-creatinine ratio (UACR)—were reviewed and described as having strong predictive power to identify patients with CKD at high risk. Data show that eGFR and UACR were multiplicatively associated with risk of all-cause and cardiovascular mortality, with eGFR <60 mL/minute/1.73 m^2 and UACR >1.1 mg/mmol (10 mg/g) as independent predictors of mortality risk in the general population [Chronic Kidney Disease Prognosis Consortium. *Lancet* 2010].

Dr. Schmieder emphasized that estimation of GFR is essential for both the staging and the management of CKD (Table 1) [National Kidney Foundation. *Am J Kidney Dis* 2002].

Table 1. Importance of GFR for Appropriate Staging and Management of Chronic Kidney Disease

Stage	Description	GFR[a]	US Prevalence	Action
1	Kidney damage with normal or ↑ GFR	≥90	5 900 000	Diagnosis and treat; treat comorbid conditions; reduce cardiovascular risk
2	Kidney damage with mild ↓ GFR	60–90	5 300 000	Estimate progression
3	Moderate ↓ GFR	30–59	7 600 000	Evaluate and treat complications
4	Severe ↓ GFR	15–29	400 000	Preparation for kidney replacement therapy
5	Kidney failure	<15[b]	300 000	Kidney replacement if uremia present

GFR=glomerular filtration rate.

[a]mL/minute/1.73 m^2.

[b]Or dialysis.

Overall, he stated that better BP control is essential, and he highlighted that despite medical treatment, many patients have persistent uncontrolled BP [Peralta CA et al. *Hypertens* 2005; Hajjar I, Kotchen TA. *JAMA* 2003]. What is really needed, he concluded, are population-based strategies for prevention.

Peer-Reviewed Highlights From

Hypertension 2014

June 13-16, 2014
Athens, Greece

BP TARGETS IN PATIENTS WITH CKD

Gérard London, MD, Centre Hospitalier Manhès, Fleury-Mérogis Cedex, France, spoke on appropriate BP targets in patients with CKD based on the clinical practice guidelines developed by the Kidney Disease Improving Global Outcomes (KDIGO) [KDIGO. *Kidney International Supplements* 2012] He first described the process of generating and grading the recommendations as shown in Table 2.

Table 2. Final Grading of the KDIGO Recommendations

Grade	Strength/Quality	Wording
Strength of recommendation		
Level 1	Strong	"We recommend"
Level 2	Weak	"We suggest"
Quality of evidence		
A	High	
B	Moderate	
C	Low	
D	Very low	
Not graded		

KDIGO=Kidney Disease Improving Global Outcomes.

Given the lack of high-quality evidence for most of the issues discussed in the guidelines, he emphasized that most of the recommendations provided are not based on the highest quality of evidence and that many of the guidelines offered only rise to the level of suggestion. Table 3 summarizes the recommendations based on the best evidence for the management of BP in patients with CKD.

DEGREE OF RENIN-ANGIOTENSIN-ALDOSTERONE SYSTEM BLOCKAGE IN HYPERTENSIVE PATIENTS WITH CKD

Pantelis A. Sarafidis, MD, Senior Lecturer and Honorary Consultant in Nephrology, Department of Nephrology, Hippkoration Hospital, Aristotle University, Thessaloniki, Greece, spoke on the degree of renin-angiotensin-aldosterone system (RAAS) blockade in hypertensive patients with CKD. Figure 1 illustrates the role of the RAAS on renal disease.

Dr. Sarafidis then described clinical data on the effect of RAAS inhibition on renal protection, highlighting that the benefit of RAAS inhibition is mainly in patients with proteinuric nephropathies or those with diabetes and microalbuminuria (Table 4) [Sarafidis P et al. *Am J Kidney Dis* 2007].

Although data show that renin-angiotensin system (RAS) blockers reduce progression of typical diabetic

Table 3. Recommendations Based on the Best Evidence for Blood Pressure Management in Chronic Kidney Disease

Target Population	Goal, mm Hg	Evidence Level	Commentary
Nondiabetic CKD			
Normal–mild albuminuria	≤140/90	1B	Evidence based, recommend <140/90 mm Hg
Moderate–severe albuminuria	≤130/80	2D, 2C[a]	Reasonable to select a goal of <140/90 mm Hg, especially for moderate albuminuria
Diabetic CKD			
Normal–mild albuminuria	≤140/90	1B	Evidence based, recommend <140/90 mm Hg
Moderate–severe albuminuria	≤130/80	2D	Reasonable to select a goal of <140/90 mm Hg
Kidney transplant recipients	≤130/80	2D	Reasonable to select a goal of <140/90 mm Hg
Children with CKD	≤90th percentile[b]	2D	No evidence to support either recommendation
	≤50th percentile[c]		
Elderly with CKD	Individualize	NA	Reasonable to consider a higher goal, especially for age >80 years

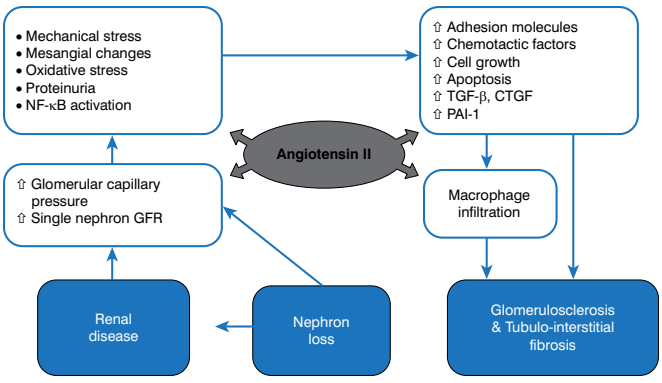
CKD=chronic kidney disease; NA=not available.

[a]2D moderate, 2C severe.

[b]For age, sex, height.

[c]For age, sex, height with any proteinuria.

Figure 1. Angiotensin II and Kidney Injury



CTGF=connective tissue growth factor; GFR=glomerular filtration rate; PAI-1=plasminogen activator inhibitor-1; TGF-β=transforming growth factor-beta.

Reproduced with permission from PA Sarafidis, MD.

Table 4. Major Randomized Clinical Trials on Renoprotective Effect of RAAS Inhibition

Study	Population (n)	Comparison	Result, %
Captopril	Diabetic nephropathy I (409)	Captopril vs placebo	45[a]
AIPRI	Mixed nephropathy (583)	Benazepril vs placebo	53[b]
REIN stratum 2	Nondiabetic nephropathy, proteinuria >3 g (1117)	Ramipril vs placebo	52[b]
REIN stratum 1	Nondiabetic nephropathy, proteinuria 1-3 g (186)	Ramipril vs placebo	56[c]
AASK	Hypertensive nephropathy suspicion (653)	Ramipril vs amlodipine	48[b]
IDNT	Diabetic nephropathy (1715)	Irbesartan vs placebo, vs amlodipine	20,[b] 23[b]
RENAL	Diabetic nephropathy (1513)	Losartan vs placebo	16[b]
DETAIL	Diabetic nephropathy (250)	Enalapril vs telmisartan	NS[d]
BENEDICT	Diabetes type 2 without microalbuminuria (1204)	Trandolapril vs placebo	47[e]

ESRD=end-stage renal disease; NS=not significant; RAS=renin-angiotensin system; SCr=serum creatinine.

[a]End point of doubling SCr only.

[b]Risk reduction for ESRD, death, or doubling of SCr or 50% reduction of clearance.

[c]Endpoint of ESRD only.

[d]Change in glomerular filtration rate after 5 years.

[e]Microalbuminuria development.

neuropathy from normo- to microalbuminuria and from micro- to macroalbuminuria, he stated that no specific agents are indicated in patients with diabetes, normoalbuminuria, and other causes of reduced eGFR (particularly in elderly patients). He also noted that elderly people are underrepresented in these clinical trials, and he emphasized the need to consider this. Specifically, RAS blockers and diuretics may increase the risk of prerenal acute renal failure in elderly persons—including other predisposed patients, such as those with renal arterial lesions or heart failure or those using radiocontrasts or nonsteroidal anti-inflammatory drugs—and that may translate into progression of CKD. For patients without diabetes and nonproteinuric CKD, he said that RAS inhibition and use of diuretics should be individualized, with close follow-up of renal function.

DIAGNOSIS AND MANAGEMENT OF HYPERTENSION IN ESRD PATIENTS

Carmine Zoccali, MD, Riuniti Hospital, Reggio Calabria, Italy, spoke on the diagnosis and management of hypertension in ESRD patients and the complex relationship between BP and outcomes in this population. Given the dips in BP in this population because of the differences in pre- and postdialysis BP, he clarified that hypertension in these patients mainly depends on volume expansion and that correcting fluid overload by long dialysis sessions in these patients reduces BP.

He indicated that because of the pre- and postdialysis fluctuations in BP based on fluid status, the use of the gold standard 24-hour BP monitoring is not reliable in this population. Instead, evidence from a joint position statement by the American Society of Hypertension and American Society of Nephrology supports estimating a first-time BP at 44 hours between 2 dialysis sessions with a new threshold for defining hypertension as 135/88 mm Hg (Agarwal R et al. *J Am Soc Nephrol* 2014). If only home monitoring is available, the guidelines recommend 48-hour monitoring, with hypertension defined as >140/90 mm Hg. He said that home monitoring is a good surrogate and is associated with better ambulatory BP monitoring than capturing pre- and posthemodialysis BP; furthermore, it tracks changes in BP evoked by reduction in body fluids, and it is more reproducible than pre- and posthemodialysis BP.

Among the interventions that he described to manage BP in this population was the use of ultrafiltration (UF) intensification, with evidence showing that UF intensification with constant dialysis duration reduces BP [Agarwal R et al. *Hypertension* 2009]. However, other data suggesting that UF intensification may increase adverse events in these patients [Curatola G et al. *J Nephrol* 2011] indicate the need for more thorough assessment via adequately powered studies to assess safety.

Reducing BP lowers cardiovascular risk in these patients, he said, but there is no evidence of pleiotropism by RAS blockade in these patients. Overall, he said that beta-blockade confers superior cardioprotection compared to angiotensin-converting-enzyme inhibition in these patients.

SESSION SUMMARY

In sum, the increasing prevalence of CKD and ESRD relates to the increasing prevalence of risk factors, such as hypertension and diabetes, and suboptimal risk factor control. RAAS blockade improves renal outcomes in patients with proteinuric nephropathies or those with diabetes and microalbuminuria. In those who have progressed to ESRD, BP typically reflects volume status. As such, a standardized approach to measurement and management of BP must take into account the time in relation to volume removal via dialysis or UF.