The Kidney in Hypertension

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KEYWORDS

• Renal • Hypertension • Kidney • Outcomes • Diabetes

KEY POINTS

- Hypertension is the second most common cause of kidney disease.
- Nephropathy progression in those with an estimated glomerular filtration rate of less than 60 mL/min/1.73 m^2 has slowed from a decline of 8 to 2 mL/min/year.
- Goal blood pressure is well below 140/90 mm Hg.

EPIDEMIOLOGY OF CHRONIC KIDNEY DISEASE

According to the Kidney Disease Outcome Quality Initiative guidelines, chronic kidney disease (CKD) is a glomerular filtration rate (GFR) of less than 60 mL/min/1.73 m^2 for longer than 3 months or other markers of kidney damage such as structural (ie, parenchymal, anatomic) or functional (ie, proteinuria, hematuria) abnormalities.[1] Although historically the Cockcroft–Gault equation has been used to calculate GFR, the more recent Modification of Diet in Renal Disease (MDRD) and CKD Epidemiology Collaboration formulas have proven more accurate, particularly with GFRs less (MDRD) or more (CKD Epidemiology Collaboration) than 60 mL/min/1.73 m^2.[2] With these equations and the severity of albuminuria, levels of kidney function and the risk of progression of kidney disease can be ascertained (**Table 1**).[3] Using data from the 13,000 individuals participating in National Health and Nutrition Examination Surveys from 1999 to 2004, 13% of those 20 years of age or older suffer from CKD as determined by the MDRD equation, with stage 3 disease being the most prevalent (7.8%; **Table 2**).[4]

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Table 1
Relative risk of progression to ESRD by eGFR (mL/min/1.73 m^2) and level of albuminuria

eGFR	ACR <10	ACR 10–30	ACR 30–300	ACR >300
>105	Reference	Reference	7.8	18
90–105	Reference	Reference	11	20
75–90	Reference	Reference	3.8	48
60–75	Reference	Reference	7.4	67
45–60	5.2	22	40	147
30–45	56	74	294	763
15–30	433	1044	1056	2286

Abbreviations: ACR, albumin to creatinine ratio; eGFR, estimated glomerular filtration rate.
Data from Levey AS, de Jong PE, Coresh J, et al. The definition, classification, and prognosis of chronic kidney disease: a KDIGO Controversies Conference report. Kidney Int 2011;80(1):17–28.

PATHOPHYSIOLOGY OF HYPERTENSION BASED ON KIDNEY DISEASE STATUS

In its simplest form, hypertension is the product of systemic vascular resistance and cardiac output (cardiac output = heart rate × stroke volume). Although numerous mechanisms have been implicated, the principal driver of increases in blood pressure involve the interwoven disorders of pressure natriuresis/salt sensitivity, dysregulation of the sympathetic and renal–angiotensin–aldosterone systems (RAAS), endothelial dysfunction, and pathologic arterial stiffness.[5] Pressure natriuresis refers to enhanced renal sodium excretion in response to increases in blood pressure such that sodium balance, and by extension blood pressure, returns to its previous state of equilibrium. In salt-sensitive states such as advanced age or CKD, salt handling is impaired, resulting in an expansion of extracellular volume, increased systemic vascular resistance, and ultimately overt hypertension (**Fig. 1**).[6] Sympathetic nervous system activation, manifest by increases in systemic catecholamine levels, leads to vasoconstriction, endothelial dysfunction, and a salt avid state.[7,8] Activation of the RAAS, specifically via the angiotensin II type 1 receptor, results in smooth muscle vasoconstriction, sodium retention, upregulation of aldosterone synthesis, fibrosis, and vascular injury.[9] At the level of the endothelium, the interplay of nitric oxide, endothelin-1, and oxidative stress figure prominently in blood pressure homeostasis. Endothelial production of the vasoactive peptide nitric oxide results in vascular smooth muscle relaxation, a process stimulated by flow (ie, blood pressure) induced shear stress.[10] However, nitric

Table 2
Prevalence of CKD by stage among US adults

CKD Stage	Prevalence (%)
1	1.8
2	3.2
3	7.7
4	0.4
5	NA

Abbreviation: CKD, chronic kidney disease.
Data from Coresh J, Selvin E, Stevens LA, et al. Prevalence of chronic kidney disease in the United States. JAMA 2007;298(17):2038–47.