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# Epidemiology of Hypertension in the Elderly With Chronic Kidney Disease

Michael J. Fischer and Ann M. O'Hare

**As the population of the United States ages, the prevalence of age-related chronic conditions such as hypertension and chronic kidney disease (CKD) will also increase. Available studies in nationally representative samples and select outpatient populations indicate that hypertension is very common in older adults with CKD, and despite the use of medication it is often poorly controlled. Generally, less than one-third of the elderly patients with CKD achieve a level of blood pressure control consistent with that of the current guideline recommendations. However, limited evidence is available from observational studies and clinical trials to inform management of hypertension in the elderly population with CKD. The available published data suggest that the relationship between clinical outcomes and the treatment of hypertension among older adults with CKD is complex and distinct from that of their younger counterparts. Larger and more robust analyses are needed for a better understanding of the association between hypertension, its treatment, and clinical events in elderly patients with CKD.**

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The population of United States (U.S.) is aging. According to the recent U.S. Census Bureau estimates, 12% of Americans are 65 years of age or older and the rate of growth of this subgroup has been exceeding others.<sup>1</sup> By the middle of the 21st century, it is projected that the number of elderly Americans ( $\geq 65$  years) will double so that nearly 1 in 5 Americans will be 65 years or older.<sup>1</sup> In fact, men and women aged  $>85$  years, the very elderly, constitute the fastest growing segment of the U.S. population.<sup>1</sup> As the mean age of the population increases, the prevalence of age-related chronic conditions, such as hypertension and chronic kidney disease (CKD), will also increase.<sup>2</sup> Moreover, rates of hospitalization and healthcare expenditures can also be expected to rise dramatically over the next 50 years.<sup>2</sup>

The prevalence of CKD and end-stage kidney disease (ESKD) has been consistently observed to be higher in the elderly population. In a representative sample of the U.S. population, less than 5% of individuals aged 20 to 39 years had moderately or severely decreased kidney function (estimated glomerular filtration rate [eGFR]  $<60$  mL/min/m<sup>2</sup>), compared with more than 40% of U.S. adults aged  $>70$  years.<sup>3</sup> Similarly, in a national sample of individuals using Veterans Affairs healthcare services, CKD was found in less than 15% of veterans aged  $<65$  years, as compared with nearly 50% of veterans aged  $>85$  years.<sup>4</sup> The prevalence and incidence of ESKD treated with dialysis or transplant are also heavily

age-dependent. The mean age at start of chronic ESKD therapy in the U.S. is 62.8 years, which has slowly risen over the last 3 decades.<sup>5</sup> As compared with those aged  $<60$  years, incidence rates of treated ESKD have been noted to be more than 2-fold and 3-fold higher in individuals aged 65 to 69 and 80 to 84 years, respectively.<sup>5</sup> Among adults aged  $>85$  years, the incidence of treated ESKD appears to decrease with age, perhaps reflecting age differences in rates of dialysis acceptance.<sup>6</sup> Nevertheless, even in these very elderly patients, the incidence of treated ESKD has increased over the past decade.

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*From Medicine/Nephrology, Jesse Brown VA Medical Center, University of Illinois Medical Center, Chicago, IL; Center for Management of Complex Chronic Care, Edward Hines, Jr. VA Hospital, Hines, IL; and VA Puget Sound Healthcare System, University of Washington, Seattle, Washington, DC.*

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*Address correspondence to Michael J. Fischer, MD, MSPH, Center for Management of Complex Chronic Care, Hines VA Hospital and Jesse Brown VAMC, 5000 S. 5th Ave (151H), Hines, IL 60141. E-mail: fischerm@uic.edu*

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Similar to CKD, the prevalence of hypertension, especially systolic hypertension, also increases with age across race, ethnic, and gender groups.<sup>7</sup> Studies in a variety of different populations, including studies in samples representative of the U.S. population, community-based studies, and managed care organizations, have consistently noted a graded increase in the prevalence of hypertension with advancing age, primarily reflecting an age-related rise in systolic blood pressure.<sup>7-9</sup> In fact, over time, the prevalence of hypertension appears to be increasing most rapidly in individuals aged  $\geq 60$  years. In these older adults, rates of hypertension control have improved little over time and remain much lower for their younger counterparts.<sup>10</sup> In a representative sample of U.S. adults, the prevalence of hypertension (blood pressure  $\geq 140/90$  mm Hg or use of antihypertensive medications) was 65.4% and adequate control of hypertension (blood pressure  $< 140/90$  mm Hg) was only 27.4% in those aged 60 and older compared with 30.1% and 41.6%, respectively, in those aged 40 to 59 years.<sup>10</sup>

CKD and hypertension are known to be strongly interrelated chronic conditions. The kidneys are well recognized to have a fundamental role in blood pressure regulation.<sup>11-13</sup> Evidence from animal studies has consistently demonstrated that kidney injury leads to the development of hypertension.<sup>11-13</sup> Moreover, data from human studies have linked reduced nephron number and reductions in eGFR within the normal range with an increased risk of hypertension.<sup>14-16</sup> Conversely, it is widely accepted that hypertension is a leading contributor to progression of kidney disease and development of ESKD.<sup>17</sup> Although aging is known to facilitate the development of both hypertension and CKD,<sup>3-10,18</sup> it is less clear whether aging affects the relationship between these 2 chronic conditions.

In the course of this review, we will characterize the current understanding of the relationship between hypertension and CKD in older adults and examine the existing epidemiologic literature regarding hypertension in older adults with CKD and discuss its clinical implications for this vulnerable population. It is important to recognize that comparing

results of studies examining the relationship between kidney function and blood pressure across age groups is challenging because of heterogeneity in both source population and study design, age of participants included, definitions of CKD and hypertension, and outcomes selected for analysis.

### Prevalence of CKD Across Strata of Blood Pressure in the Elderly Population

One of the first studies to examine the relationship between blood pressure, CKD, and age was conducted using data from the Third National Health and Nutrition Examination Survey (NHANES III) by Coresh and colleagues (Table 1).<sup>19</sup> In this analysis of a representative sample of the adult U.S. population from 1988 to 1994, the prevalence of CKD generally increased with higher blood pressure levels among individuals *untreated* for hypertension. However, among older members of this *untreated* group (age  $\geq 60$  years), a J-shaped relationship existed between CKD and strata of blood pressure (Table 1). The prevalence of CKD was lowest at a systolic blood pressure 120 to 159 mm Hg and a diastolic blood pressure 80 to 99 mm Hg and higher at either systolic blood pressure  $< 120$  mm Hg and diastolic blood pressure  $< 80$  mm Hg or systolic blood pressure  $\geq 160$  mm Hg and diastolic blood pressure  $\geq 100$  mm Hg. In those *treated* for hypertension (both the overall sample and in the subgroup of elderly [ $\geq 60$  years]), there was a J-shaped relationship between elevated serum creatinine and blood pressure.

Rao and colleagues examined the relationship between hypertension and CKD among participants from both the Kidney Early Evaluation Program (KEEP) 2000 to 2006 and NHANES 1999 to 2004 (Table 1).<sup>20</sup> Among participants with hypertension in both KEEP and NHANES, older age was associated with a graded increase in the prevalence of CKD and in the frequency of more severe CKD (Table 1). As compared with an approximate 21% prevalence of CKD in hypertensive KEEP participants  $\leq 45$  years, over 58% of hypertensive KEEP subjects  $> 75$  years had CKD, the vast majority having stage 3 to 5 CKD. In

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