
Diagnosis and Treatment of Glomerular Diseases in Elderly Patients

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Glomerular diseases are common in elderly patients and are a major cause of kidney failure. Most glomerular diseases in the elderly are caused by chronic systemic diseases, including arterial hypertension, diabetes, and atherosclerotic vascular diseases, although acute systemic vasculitis, especially anti-neutrophil-cytoplasmic-antibody-mediated vasculitis, and membranous nephropathy related to malignancy, drug toxicity, and idiopathic form also occur often. Complex age-related changes and sensitivity to drug toxicity can render diagnosis and treatment for elderly patients challenging. As the general population is aging and the rate of CKD rising, updating knowledge on managing these patients is critical for care providers. We provide a comprehensive review and update of the diagnosis and treatment of glomerular diseases in the elderly.

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Introduction

Recent data show that the prevalence of CKD is fast rising and is highest (up to 38%) in patients older than 65 years of age.¹⁻⁵ Most glomerular diseases in the elderly are caused by chronic hypertension, diabetes, and glomerular ischemia, although elderly patients can also suffer from other primary and/or secondary glomerular diseases. Aging itself is well known to be associated with progressive decline in kidney reserve⁶; 30% of the glomeruli are obsolete because of sclerosis in clinically healthy individuals by age 75,⁷ and kidney inulin clearance drops by almost half, from 122.8 to 65.3 mL/min per 1.73 m², between the ages of 20 and 29 and 80 or older.⁸ Cellular changes (eg, decline in the length of telomere and antiaging factor [Klotho]), as well as inherited predisposing factors (small number of glomeruli and glutathione S-transferase mu 1 genotype) can all be in play in aging-related kidney dysfunction.⁹⁻¹²

Kidney biopsy is an important part of clinical care for patients with glomerular diseases. Over the last few decades, the rate of kidney biopsy in elderly patients has increased substantially.¹³⁻¹⁵ This is attributable, at least in part, to the recognition that kidney biopsy for the elderly is not associated with an elevated rate of complications compared with that in younger adults,¹⁵⁻¹⁸ and, more importantly, it is clinically informative.^{15,17,18} Moutzouris and colleagues showed that up to 67% of very elderly (>80 years of age) had a change in treatment strategy in light of the biopsy findings,¹⁵ presumably affecting dis-

ease outcome. Kidney biopsy also offers prognostic information and eliminates potential overtreatment, which can cause therapy-related toxicities.

In most publications, the distribution of glomerular diseases in the elderly is derived from kidney biopsy series. Thus, the distribution can be biased because of nonhomogeneous referral patterns and biopsy policies. Bias toward the elderly can include reluctance in performing biopsy because of age and inconsistency in preferred indications for kidney biopsy, which differ considerably from region to region. For instance, in South America and Europe, the major indication for kidney biopsy has been proteinuria with or without serum creatinine elevation. However, in the United States, indications tend to be those with varying degrees of systemic or extrarenal manifestations, nephritic syndrome, and serum creatinine elevation. Therefore, it is not surprising that in large registry studies from Europe and South America, the most frequent biopsy finding of parenchymal diseases in the elderly tends to be membranous nephropathy (MN),^{13,14,19,20} whereas pauci-immune necrotizing and crescentic glomerulonephritis has been the most frequent biopsy finding in the United States.^{15,18} An exception is in the very elderly, in which pauci-immune necrotizing and crescentic glomerulonephritis is consistently the most common biopsy finding.^{15,18,20} In practice, most glomerular diseases in elderly patients are secondary and attributable to various chronic systemic diseases and comorbidities. Primary (idiopathic) glomerulonephritis represents a minority of glomerular diseases in the elderly.

Pathologically, in addition to features of specific glomerular diseases, kidney biopsy from elderly patients often shows aging-related features including varying degrees of background glomerulosclerosis, tubular atrophy, interstitial fibrosis, arterial sclerosis, and arteriolar hyalinosis. Distinguishing a newly developed glomerulopathy from underlying age-associated kidney senescence can, at times, be challenging.

From a treatment standpoint, age-related decline in the capacity of drug metabolism and excretion^{21,22} can engender susceptibility to drug accumulation and

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toxicities, especially to immunosuppressants. These problems can be further compounded by the ongoing loss in muscle mass, generalized deconditioning, and an increase in frailty, which can result in a seemingly near-normal serum creatinine. In reality, these patients may have moderate to severe loss of kidney function. The number of elderly patients being initiated on dialysis has grown considerably over the past decade.²³ Survival of elderly dialysis patients is heavily influenced by the degree of comorbidity.²⁴ A new comorbidity index²⁵ was recently proposed and shown to effectively predict mortality rates for elderly dialysis patients.²⁴ Age alone should not be used against initiation of dialysis. Here, we comprehensively review diagnosis and treatment of glomerular diseases in elderly patients, incorporating current literature and treatment guidelines.

Glomerular Diseases Associated With Chronic Hypertension

Hypertension is common in elderly patients. Lifetime risk for hypertension in an individual over the age of 55 is more than 90%.^{26,27} More than 2/3 of patients over the age of 65 have hypertension, with approximately 60% having isolated systolic hypertension.^{28,29} Hypertension, including isolated systolic hypertension, is a major risk factor for coronary artery events, stroke, congestive heart failure, peripheral vascular disease, and kidney failure³⁰ in the elderly, and it increases cardiovascular mortality.^{29,31,32} Despite the high occurrence, older patients have the lowest rate of blood pressure (BP) control compared with younger patients. Only 36% of men and 28% of women aged 60 to 79 years and 38% of men and 23% of women aged above 80 years had optimal BP control.³³

Primary hypertension accounts for more than 90% of elderly BP elevation. The underlying pathophysiology is thought to be related to an age-associated increase in arterial stiffening due to structural changes within the arterial wall, including intimal fibrosis, vessel wall calcification, and degradation of elastic fibers.^{34,35} Depending on individual health status, additional factors such as endothelial dysfunction, cardiac dysfunction related to myocardial remodeling, autonomic dysregulation, and concurrent kidney insufficiency may all contribute to the genesis of hypertension in elderly.³⁶ Secondary hypertension accounts for fewer than 10% of cases. The leading secondary causes are CKD and atherosclerotic renal artery stenosis (ARAS). Other causes include

obstructive sleep apnea; hyperaldosteronism; thyroid dysfunction; and, rarely, pheochromocytoma and intracranial disorders.

Resistant hypertension, occurring in approximately 8% to 15% of patients with hypertension (defined by the Seventh Report of the Joint National Committee²⁷; **Table 1**), refers to a BP of more than 140/90 mmHg while on 3 optimally dosed antihypertensive agents with 1 being a diuretic. Risk factors for resistant hypertension include old age, Black race, obesity, CKD, elevated risks of coronary heart disease, nonadherence to antihypertensive regimen, excess sodium intake, deficient potassium intake, smoking, and ingestion of certain over-the-counter or recreational vasoconstrictive drugs.^{37,38}

The histologic changes associated with benign chronic hypertension are called “hypertensive arterionephrosclerosis” and are similar to age-related arterionephrosclerosis. These include variable degrees of arterio- and arteriolosclerosis with hyalinosis, secondary focal global glomerulosclerosis, and glomerular ischemic changes.

Few patients develop secondary focal segmental glomerulosclerosis (FSGS), which is heralded by significant proteinuria. In the elderly, chronic hypertension is the most common secondary cause of FSGS.

The treatment goals are to control BP to less than 140/90 mmHg for all hypertensive patients and less than 130/80 mmHg for those with diabetes and CKD as well as to timely manage hypertension-related complications.

For elderly patients, the precise BP target is undefined, although treatment benefit has been demonstrated unequivocally in HYVET (Hypertension in the Very Elderly Trial). In HYVET, 3845 patients aged 80 years or older with a systolic BP of 160 mmHg or greater were randomly assigned to treatment vs placebo and followed for 1.8 years. Hypertensive treatment reduced the incidence of fatal and nonfatal stroke by 30%, all-cause mortality by 21%, deaths due to cardiovascular disease by 23%, and heart failure by 64%.³⁹ One caveat is that HYVET excluded elderly patients residing in nursing homes and with CKD or heart failure, making the trial results not readily applicable to a considerable portion of elderly hypertensive patients. In practice, a BP target is usually set based on the individual patient’s general health condition and comorbidities including dementia, orthostasis, and cardiovascular dysfunction.

To minimize polypharmacy and drug-related adverse effects, lifestyle modifications should be emphasized for

CLINICAL SUMMARY

- Glomerular diseases are common in the elderly.
- Kidney biopsy for elderly patients is not associated with an elevated rate of complications and can be clinically informative.
- Therapeutic recommendations for elderly patients are mostly extrapolated from younger adults.
- Treatment for elderly with glomerular diseases should be individualized. General health, cognitive function, competing comorbidities, life expectancy, and patient’s preference should all be taken into consideration.

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