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Changes and Diseases of the Kidney in Old Age

Yaşlılıkla Birlikte Böbrekte Görülen Değişimler ve Hastalıklar

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ÖZ

Yaşlanma, böbrekler de dâhil olmak üzere tüm organları etkileyen kaçınılmaz bir biyolojik süreçtir. Bu derlemenin amacı, yaşlanma sürecinde böbreklerde meydana gelen yapısal ve fonksiyonel değisiklikleri ve bu değisikliklerin klinik yansımalarını incelemektir. Yaşlı nüfusta kronik böbrek hastalığının prevalansı yüksektir ve bu durum, diyabet ve hipertansiyon gibi ek koşulların etkisiyle böbrek hasarına yatkınlığı artırmaktadır. Yaşlanmanın böbrek fonksiyonları üzerindeki etkilerini anlamak, yaşlı hastalarda böbrek hastalıklarının tanısı, tedavisi ve yaşam kalitesinin iyileştirilmesi açısından kritik öneme sahiptir. Avrıca, vasa bağlı böbrek değisiklikleri ve bu değişikliklerin sağlık sonuçları üzerine rehberlik sağlayacak bilgiler sunmaktır.

Anahtar Kelimeler: Yaşlanma, böbrek, böbrek fonksiyonu, böbrek anatomisi, böbrek hastalıkları.

ABSTRACT

Aging, an inevitable biological process, affects all organs, including the kidneys. This review delves into the structural and functional changes in the kidneys during aging and their clinical implications. With a high prevalence of chronic kidney disease in the elderly, understanding the effects of aging on renal function becomes a crucial tool in diagnosing and treating kidney diseases, thereby enhancing the quality of life in elderly patients. This understanding provides valuable guidance on age-related renal changes and their health consequences, empowering medical professionals to make informed decisions.

Keywords: Aging, kidney, kidney function, kidney anatomy, kidney diseases.



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Introduction

Aging is an inevitable biological process that significantly affects all organs and kidneys. The aging process leads to progressive loss of nephrons, glomerular and tubulointerstitial damage, and decreased renal function. These changes begin in the fourth decade of life and increase in the fifth and sixth decades, affecting glomerular-tubular function, systemic hemodynamics, and body homeostasis. The structural and functional changes in the kidneys with aging reduce their ability to adapt to changing conditions during illness or stress. Therefore, conditions that younger individuals easily tolerate may lead to fluid-electrolyte imbalances and renal failure in the elderly.¹

The elderly represent a rapidly growing population, and the prevalence of chronic kidney disease is high in this group. Older individuals are predisposed to kidney damage due to diabetes mellitus, hypertension, glomerular and tubulointerstitial diseases, as well as age-related decreases in glomerular filtration. A significant number of elderly patients reach end-stage renal failure, requiring renal replacement therapy. Older patients are often referred to a nephrologist late and have a shorter survival on renal replacement therapy than younger individuals. This group of patients has many comorbid conditions, including cardiovascular disease, malnutrition, visual and hearing problems, depression, and mental deficiency. The elderly have difficult vascular access to dialysis and are often candidates for renal transplantation. Despite all these obstacles, diagnostic and therapeutic approaches should not be considered independent of the younger population, considering the age factor. When renal diseases are diagnosed and treated, many older adults experience significant improvements in quality of life. Recognizing the changes that occur with aging will enable prevention and better treatment of clinical problems that are more common in the elderly.¹

This review aims to investigate the structural and functional effects of aging on the kidneys, protect renal health in elderly individuals, and examine the anatomical and physiological changes that occur with aging. It also aims to contribute to the literature and clinicians by examining possible diseases in the kidney with aging.

Definition of Old Age

Aging is a complex and frequently discussed concept in gerontology and geriatrics. This concept can be defined from various angles by considering its biological, psychological, and sociological dimensions. While aging refers to the processes of change in living organisms over time, old age defines a specific period. "Aging" includes the wear and tear and deterioration of living organisms over time, while it is also a process in which repair and reconstruction mechanisms are activated. Aging is a natural process that ends with death for every living being. The elderly population is rapidly increasing worldwide and in Turkey. The World Health Organization predicts that by 2025, 1.2 billion people worldwide will be 60 or older. In Turkey, the ratio of the elderly population to the total population increased from 3.4% in 1955 to 7.1% in 2010.²

Biological Process in Old Age

Old age is the changes that occur after reaching adulthood in terms of biological functions, from the end of the reproductive period until death. One of the most important changes in this period is the decrease in fertility and the increase in mortality. While old age refers to the changes seen with chronological age, with its psychological dimension, it includes the change in human adaptive capacity in terms of perception, learning, psychomotor, problem-solving, and personality characteristics.²

Effects of Genetic Factors on Kidney Aging

In the context of the progression of age-related renal disorders in experimental models, it is increasingly recognized that both sex and the overall genetic background play important roles.³ Sex is





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one of the determinants of the rate of progression of age-related decline in renal function.⁴ In male animals, much of the damage to the kidney with aging is associated with androgen production, and medical castration may slow the progression of these changes.⁵ At the same time, treatment with estrogen-containing compounds may prevent the progression of age-related kidney disease.⁶

One of the notable developments among age-related genes is the klotho gene, which is significantly down-regulated in chronic renal failure. Klotho is a gene highly expressed in the kidney and responsible for the accelerated aging phenotype. Klotho expression is central to calcium and phosphorus homeostasis and negatively regulates active vitamin D synthesis. It has been suggested that angiotensin II down-regulates klotho expression, which may cause accelerated angiotensin II-associated kidney damage.⁷

In many different human diseases, it is argued that not only gender but also genetic background has a key influence on the age of onset, severity, and rate of progression. Clotho polymorphisms are associated with osteopenia in postmenopausal women.⁷ Similar to kidney disease in humans, racial background is also influential in protecting against and predisposing to specific diseases. For example, African Americans have been shown to have an increased susceptibility to hypertensive nephrosclerosis.⁸

Anatomical Changes in the Kidney Due to Aging

There is a decrease in kidney mass with advancing age. Kidney mass, which is 200-270 grams at the age of thirty, decreases by 20%-30% to 180-200 grams at 90.9 During this mass loss, the medulla tissue is preserved, and the loss is mainly due to the cortex tissue. Along with the change in renal mass, the glomeruli also decrease with aging. Sclerosis or hyalinization in glomeruli starts at the age of 30. While the rate of entirely sclerosed glomeruli in light microscopy is 1-2% at the age of 30, this rate reaches 10-12% at the age of 70. 12,13

When the glomerular structure is examined microscopically, it is observed that the basement membrane thickens, and the glomerular surface cross-sectional area decreases with aging. ^{10,14} Interstitial fibrosis is another anatomical change that occurs with aging. ¹⁵ In the absence of hypertension or other systemic diseases affecting the kidney, intimal thickening and accompanying sclerotic changes occur in arteriole and large vessel walls with aging. ¹⁶

Vascular changes in the kidney due to aging

Macrovascular diseases, such as atherosclerotic diseases of the aorta and renal arteries in the aging process, are associated with cholesterol embolism and parenchymal injury. Scar tissue resulting from this mechanism can be difficult to identify because cholesterol is soluble in commonly used solvents and lesions may be small. Intrarenal arterial changes in the aging kidney resemble vascular disease seen in systemic diseases, arteriolosclerosis, and hypertrophy of the intima and media. Fibrointimal hyperplasia is common in renal biopsies and is even present in normal individuals without cardiovascular disease. Fibrointimal hyperplasia is more prominent in the interlobular arteries. Hypertension accelerates this process, but it is impossible to distinguish morphologically between intimal hyperplasia associated and not associated with hypertension. Since this condition is commonly present in almost all elderly patients, it is very difficult to interpret the renal dysfunction seen as "hypertensive nephropathy clinically." These vascular changes lead to local tubular atrophy and interstitial fibrosis. These vascular, tubular, interstitial, and glomerular changes result in hyperfiltration injury followed by segmental and global glomerulosclerosis. This results in compensatory hypertrophy of the medullary glomeruli. A 1 picometer increase in arterial thickness is estimated to result in a 1.6 mm/Hg increase in mean blood pressure. However, whether these vascular changes occur before or after hypertension is still controversial.¹⁷





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Physiological Changes in the Kidney Due to Aging and Clinical Effects

Significant changes occur in renal physiology during the aging process. Renal plasma flow, which is approximately 600 ml/min at the age of 30 years, decreases by 10% per decade to 30 ml/min at the age of 80 years. In studies, it has been observed that blood flow in kidney donors decreases more markedly in the cortical region while medullary blood flow is preserved. Increases in resistance in both afferent and efferent arterioles accompany this decrease. Increased efferent arteriole resistance and relative preservation of blood flow in juxtamedullary nephrons with high filtration fraction led to increased filtration fraction with aging. Studies have shown that the vasodilator response of the kidney to acetylcholine is decreased in the elderly compared to the young, but the vasoconstrictor effect of angiotensin is unchanged. 19,20

Glomerular filtration rate (GFR) decreases by an average of 0.8 ml/min per year from the age of 30.²¹ This decrease is reportedly more pronounced, especially in the black race.²² At first, it was thought that glomerular hyperfiltration occurring in nephrons decreasing with aging could lead to a progressive renal dysfunction. However, animal studies have shown that the glomerular filtration rate in a single nephron does not change with aging.²³ Therefore, the decrease in glomerular filtration rate is only associated with decreased nephrons due to anatomical changes.

Serum creatinine level should not be considered a reliable indicator of decreasing glomerular filtration rate with age because muscle mass decreases similarly with aging. At 25 years, muscle mass is 19% of body weight, whereas at 70 years, this ratio decreases to 15%.21 Therefore, this should be taken into account when adjusting drug dosage in elderly patients, and it should be taken into account that a decrease in glomerular filtration rate may be observed without a significant increase in serum creatinine level.²⁴

Decreased glomerular filtration and blood flow lead to a higher risk of prerenal acute renal failure in older individuals than in younger ones.²⁵

Congestive heart failure, vomiting, diarrhea, gastrointestinal bleeding, significant surgeries, and unconscious diuretic use are common causes of prerenal acute renal failure in the elderly. Without early intervention, acute tubular necrosis can often develop. In addition, the elderly are at increased risk of acute renal failure due to aminoglycosides and radiocontrast agents. Decreased adequate plasma volume or the presence of atheromatous ischemic kidney disease in the elderly, nonsteroidal anti-inflammatory drugs, and angiotensin-converting enzyme inhibitors frequently used in this age group may lead to renal dysfunction and acute renal failure.²⁶

Structural Changes Occurring in Glomeruli Due to Aging

During the aging process, the number and percentage of sclerosed glomeruli increase along with the decrease in the number of glomeruli. It is estimated that about 10% of glomeruli are lost by age 40. Subcapsular cortical glomeruli are more prone to sclerosis than juxtamedullary glomeruli. Glomerular sclerosis is thought to be a nonspecific end-stage morphologic change resulting from injury, such as ischemia and a wide range of immunologic disorders. However, different stimuli have been demonstrated to cause different segmental sclerosed lesions. In addition to changes in the number of glomeruli, there is an increase in the volume of the glomerular basement membrane and mesangial matrix. These changes will likely result from changes in the balance between extracellular matrix production and degradation in the glomerulus.¹⁷

Endothelial changes occur with aging, which may lead to vasoconstriction that predisposes to ischemia. During the aging process, the vascular endothelium produces less prostacyclin and nitric oxide, which is associated with a decrease in endothelial nitric oxide synthase production in the peritubular capillary endothelium. In addition to the loss of normal endothelial vasodilator substances,





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an increase in renal vasoconstrictor substances such as angiotensin II, endothelin-1, and nitro-L-arginine methyl ester (a nitric oxide synthase inhibitor) is also observed.²⁷

Prolonged hyperuricemia is similar to the renal functional and histological changes observed during aging. It is of interest that experimental hyperuricemia causes glomerular hypertrophy, glomerulosclerosis and tubulointerstitial fibrosis.²⁸

Pathogenesis of Progressive Kidney Diseases in Old Age

During the aging process, the number of glomeruli has been shown to decrease from approximately one million in each kidney to 600,000 or less by the eighth decade. The loss of nephrons results in hyperfiltration, which leads to glomerular hypertrophy, resulting in increased glomerular hydrostatic pressure and the development of scar tissue in the glomeruli.²⁹ However, aging studies in rats have revealed that kidney damage begins independently of glomerular hypertension. Indeed, depending on the species, glomerular hydrostatic pressures may be normal or increased with aging.³⁰ Thus, it is likely that glomerular hypertension resulting from a decrease in nephron mass is a co-factor rather than an initiator of structural renal changes in the aging process.

Common Kidney Diseases in Old Age

Glomerular Diseases

Diabetic nephropathy is one of the leading causes of chronic kidney disease and end-stage renal failure in adults aged 60 years and older.³¹ Since 1995, the incidence of end-stage renal failure from diabetic nephropathy has generally decreased. This can be attributed to tight blood pressure control, renal protection strategies with blockade of the angiotensin system, and improved glycemic monitoring and treatment.¹ Another important cause is hypertensive nephrosclerosis. Uncontrolled hypertension can lead to an acceleration of renal dysfunction in other kidney diseases. Although diabetic nephropathy is the most common cause, secondary glomerular diseases such as amyloidosis, membranous nephropathy, post-streptococcal glomerulonephritis, Wegener's granulomatosis, membranoproliferative glomerulonephritis are also observed with increasing frequency in elderly individuals. 32,33 Wegener's granulomatosis and other pauci-immune necrotizing glomerulonephritis are common in the elderly and are usually characterized by rapid onset of renal failure, erythrocyte cilia, and systemic manifestations.³⁴

In elderly individuals, amyloidosis should be considered in the presence of nephrotic syndrome with partially preserved renal function, normal or low levels of erythrocytes in urine sediment, low blood pressure, and hepatomegaly. Furthermore, the relationship between solid tumors and glomerulonephritis should be defined, as both conditions are common in the elderly, and successful treatment of the underlying malignancy can often cure glomerulonephritis.³⁵ Membranous nephropathy is usually idiopathic and may be associated with malignancies such as gastrointestinal, breast, or lung cancers. Focal segmental glomerulosclerosis is seen in all age groups and is particularly common in African Americans. Chronic lymphocytic leukemia is common in older men and may be associated with membranoproliferative glomerulonephritis. Although minimal change in disease is usually seen in children, a second peak incidence has been observed in older individuals.²⁸

Renovascular and Atheroembolic Diseases

The frequency of renovascular and other embolic diseases increases with aging. If hypertension and high serum creatinine levels are present in elderly individuals with a history of vascular disease, renovascular disease should be considered.²⁸



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Acute Renal Failure

The decrease in renal blood flow and glomerular filtration rate with aging increases the sensitivity to steroidal inflammatory drugs, angiotensin receptor antagonists, and diuretics, with increased sensitivity in elderly individuals. In addition, the frequency of conditions such as arrhythmia, other embolic disease, cardiac surgeries, and prostatic hyperplasia in the elderly may also increase the incidence of acute renal failure.³⁶ The evaluation of acute renal failure in the elderly should reflect the approach in other age groups.³⁷ A careful history and physical examination considering pre and postrenal causes should be performed with appropriate laboratory findings. After the exclusion of prerenal and postrenal causes, intrarenal causes should be identified. Acute tubular necrosis due to ischemic (hypotension) or nephrotoxicity (e.g., contrast media exposure and aminoglycoside use) is considered a common cause in the elderly. It has been found in 27% of patients over 65 years of age and 14% of patients over 60 years of age undergoing biopsy.³⁸

Furthermore, vascular involvement in the form of atheroembolism affected 7.1% of these patients. The most common pathologic finding in patients over 60 years of age undergoing biopsy for acute renal failure was pauci-immune crescentric glomerulonephritis, which occurred in 31% of cases.³⁹

Tubulointerstitial Diseases

There is an increase in the frequency of renal damage with tubulointerstitial pattern in elderly individuals. 40 Acute tubulointerstitial nephritis usually presents with fever, skin rashes, peripheral eosinophilia, and pyuria and is often due to drug toxicity. Antibiotics such as beta-lactams, sulfonamides, cephalosporins, and diuretics can cause this type of damage. Chronic tubulointerstitial nephritis usually has a painless course and is often associated with NSAID use. Tubulointerstitial nephritis is associated with other toxic agents such as viral infections, heavy metals, nephrotoxic plants, metabolic disorders, and radiation. Biopsy data from the elderly population show that 18% of cases are interstitial nephritis. This rate may not reflect the actual rate because not all patients undergo a biopsy. Exposure of elderly individuals to many medications is a possible explanation for this increase. 40

Urinary Tract Infections

The frequency of asymptomatic bacteriuria increases with aging. While the prevalence is 5% in women under the age of 50, it rises to 21% in outpatient women over the age of 65 and 53% in women in nursing homes. In men under 50 years of age, the prevalence increases from 0% to 12% in outpatients over 65 years of age and 37% in men in nursing homes. This increase may be associated with the risk of prostatic hypertrophy. Furthermore, chronic catheter use in the elderly is associated with increased bacterial colonization. Treatment of urinary tract infections is usually based on symptoms such as fever, dysuria, and increased leukocyte count. A more careful approach is required in high-risk individuals such as patients with structural defects, frequent and recurrent infections, planned urologic surgery, neutropenic patients, and renal transplant patients.²⁸

Evaluation of Hematuria and Obstructive Uropathy

Urinary tract malignancies are more common in older people. Bladder cancer is rare in men under 40 years of age and is also rare in women, but its prevalence increases from the fourth decade onwards. Renal cell carcinomas usually occur in the seventh decade, with an average age at diagnosis of 66 years and an average age at death of 70 years. Therefore, in the case of micro- or macrohematuria, the lower and upper urinary tracts should be visualized.²⁸



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Conclusion and Recommendations

This study reveals that aging significantly affects the structural and functional properties of the kidneys. In particular, a marked decrease in glomerular filtration rate, a decrease in renal plasma flow and vascular changes were observed in elderly individuals. This suggests that renal function is severely impaired in the elderly, resulting in increased susceptibility to kidney diseases. In this context, proactive approaches are needed to protect kidney health in older people. First, regular kidney function monitoring and early detection strategies should be implemented. Blood pressure management is critical to slow the progression of kidney diseases and prevent complications.

Adopting a multidisciplinary treatment approach and individualizing treatment plans by considering age-specific clinical changes may contribute to better outcomes in treating elderly patients. This review will contribute to the literature and research.

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