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Acute Kidney Injury in the Elderly

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Abstract

Acute kidney injury (AKI) is a significant clinical concern in the elderly, marked by heightened incidence rates, increased morbidity and mortality, and impaired kidney repair mechanisms. AKI often has severe consequences, including extended hospital stays, heightened rates of chronic kidney disease, and elevated healthcare costs. The vulnerability of elderly individuals to AKI is amplified by age-related structural and functional changes in the kidneys, reduced physiological reserve, and increased exposure to nephrotoxic agents. The impaired kidney repair mechanisms observed in the elderly pose further complexities in AKI management. With age, the regenerative capacity of the kidneys diminishes, resulting in incomplete recovery and long-term renal dysfunction. Therefore, identifying strategies to promote effective kidney repair and regeneration in the elderly is crucial. Investigations into age-related factors such as cellular senescence, oxidative stress, and inflammation will provide valuable insights into AKI pathogenesis and facilitate the development of targeted interventions. Furthermore, understanding the interplay between gender differences and comorbidities in AKI among the elderly necessitates ongoing research.
Introduction

Acute kidney injury (AKI) is a critical condition characterized by a sudden decline in renal function, resulting in the inability of the kidneys to adequately excrete waste products and maintain fluid and electrolyte balance (Yokota et al. 2018). It is a significant medical problem as the incidence of AKI is progressively rising and is associated with significant morbidity, mortality, and healthcare costs (Santoro, 2019). In the United States, the annual costs of AKI are estimated to be $24 billion (Matrisch et al., 2023). As a multifactorial disorder, AKI is influenced by various patient-related factors, underlying comorbidities, and environmental triggers (Mehta et al., 2015).

In the elderly, individuals aged 65 or older, for the purpose of this review, the prevalence of AKI has steadily increased due to the aging population and the rising burden of chronic diseases (Hsu & Siew, 2017).

In the clinic, age-related changes in renal structure and function, such as reduced glomerular filtration rate (GFR) and decreased renal blood flow, render the elderly more vulnerable to kidney injury, thereby resulting in a higher incidence of AKI among this population (Hommos et al. 2017). AKI in the elderly is associated with increased complication and mortality rates and prolonged hospital stays (Yokota et al., 2018). The complex interplay of age-related physiological changes, multiple comorbidities, and AKI creates a challenging scenario for healthcare providers, highlighting the need for a deeper understanding of the risk factors contributing to AKI in the elderly.

Furthermore, impaired kidney repair exacerbates the adverse outcomes of AKI in the elderly population (Chang-Panesso, 2021). Following an acute insult, such as ischemia or nephrotoxicity, the renal tubular epithelial cells initiate a repair process to restore the structural and functional integrity of the kidneys (Yokota et al., 2018). However, in the elderly, this
reparative process is often delayed, incomplete, or even absent, leading to a progressive decline in renal function and an increased risk of chronic kidney disease (CKD) development (Hommos et al., 2017). Reduced kidney repair observed in the elderly following AKI is influenced by changes in regenerative signaling pathways, increased fibrotic responses, and cellular senescence (Andrianova et al., 2021). Additionally, chronic low-grade inflammation and oxidative stress, which are more prevalent in the elderly, further hinder the regenerative processes and promote renal injury progression (Andrianova et al., 2021). By comprehending the risk factors contributing to AKI in the elderly and exploring the reasons behind decreased kidney repair, we can pave the way for targeted interventions and improved outcomes for elderly individuals at risk of or affected by AKI.

**Definition and Diagnosis of AKI**

Accurate and timely diagnosis of AKI are critical for appropriate management and intervention. In recent years, there has been a concerted effort to establish a consistent definition and set of diagnostic criteria for AKI. The Kidney Disease: Improving Global Outcomes (KDIGO) guidelines introduced in 2012 have played a pivotal role in providing standardized criteria for the identification and classification of AKI (Kellum et al., 2013). As defined by KDIGO, AKI is an abrupt decline in renal function characterized by an increase in serum creatinine (SCr) levels or a reduction in urine output. AKI is diagnosed when any of the following criteria are met: an increase in SCr by ≥0.3 mg/dL (≥26.5 μmol/L) within 48 hours, an increase in SCr to ≥1.5 times the baseline within the past seven days, or urine output <0.5 mL/kg/hour for six consecutive hours (Kellum et al., 2013).
The KDIGO guidelines also classify AKI into three stages based on the severity of renal dysfunction. Stages 1, 2, and 3, represent mild, moderate, and severe impairment respectively (Kellum et al., 2013). Each stage is defined by specific criteria and can be found in Table 1 below. Note that staging is based on the worst change in SCr or urine output. This staging criterion enables clinicians to assess the severity of AKI and guide appropriate management strategies. Staging also allows for the prediction of patient outcomes, such as the need for renal replacement therapy and the risk of mortality.

<table>
<thead>
<tr>
<th>Stage</th>
<th>Serum Creatinine</th>
<th>Urine Output</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.5–1.9 times baseline OR ≥0.3 mg/dL (≥26.5 µmol/L) increase</td>
<td>&lt;0.5 mL/kg/h for 6–12 hours</td>
</tr>
<tr>
<td>2</td>
<td>2.0–2.9 times baseline</td>
<td>&lt;0.5 mL/kg/h for ≥12 hours</td>
</tr>
<tr>
<td>3</td>
<td>3.0 times baseline OR increase in serum creatinine to ≥4.0 mg/dL (≥353.6 µmol/L) OR initiation of renal replacement therapy OR, in patients &lt;18 years, decrease in eGFR to &lt;35 mL/min per 1.73 m²</td>
<td>&lt;0.3 mL/kg/h for ≥24 hours OR anuria for ≥12 hours</td>
</tr>
</tbody>
</table>

While the KDIGO guidelines have contributed to standardizing the definition and diagnosis of AKI, it is important to note that these criteria primarily focus on changes in SCr and urine output, which may not be sensitive enough to changes in kidney function (Kuo et al., 2022). This allows for minimal changes in SCr following a significant decrease in renal function. Furthermore, there is a 48-72 hour delay in SCr changes after the initial renal injury, and can be influenced by age, sex, ethnicity, and muscle mass (Kuo et al., 2022; Mitsas et al., 2022). Additional research efforts are ongoing to explore novel biomarkers such as albuminuria and cystatin C (CysC) that are more sensitive to changes in renal function (Mitsas et al., 2022). Imaging techniques are also
being explored that can enhance early detection and improve the accuracy of AKI diagnosis. For instance, renal doppler sonography may be used to quantify renal perfusion and intrarenal hemodynamic changes to assess microstructural alterations (Lin et al., 2021). These advancements may further refine diagnostic approaches and allow for more personalized management of AKI, especially for an early warning system in the elderly.

Etiologies of AKI

An AKI is categorized as prerenal, intrarenal, or postrenal and involves disturbances in renal perfusion, direct kidney damage, or obstructive processes respectively (Kellum et al., 2021). Prerenal AKI occurs due to a reduction in renal plasma flow and GFR, leading to an accumulation of nitrogenous products in the blood (Kellum et al., 2021). This is the most common form and comprises 40-60% of AKIs (Rosner et al., 2018). The main causes of prerenal AKI include absolute volume reduction (due to hemorrhage or volume depletion), relative volume reduction (as seen in cirrhosis or heart failure), and hypoperfusion (from shock or certain medications) (Rosner et al., 2018). These conditions compromise the blood supply to the kidneys, impairing their function and increasing the risk of AKI.

Intrarenal AKIs involve direct damage to the kidney tissue itself, affecting various renal structures. Acute tubular necrosis (ATN) is the most common cause of intrarenal AKI, accounting for over 70% of cases (Rossaint & Zarbock., 2016). ATN can result from ischemic or toxic insults, leading to cellular injury and dysfunction of the renal tubules. Other less frequent causes of intrarenal AKI include tubulointerstitial nephritis, glomerulonephritis, and cortical necrosis
These conditions directly affect the kidney's structural components and can impair its ability to maintain proper filtration and excretion functions.

Postrenal AKIs involve obstructive processes that impede the flow of urine from the kidneys (Yokota et al., 2018). Obstructions can occur due to urinary tract stones, blood clots, tumors, or retroperitoneal fibrosis (Rossaint & Zarbock., 2016). Postrenal AKI is the least common type, accounting for approximately 2% to 4% of cases (Yokota et al., 2018). However, its prevalence increases with age, making it more relevant in the elderly population as up to 10% of AKIs in this age group are postrenal (Yokota et al., 2018). Timely identification and resolution of these obstructive causes are essential to prevent further renal damage and restore normal kidney function.

It is important to note that these etiologies of AKI are not mutually exclusive and can interact or overlap in some cases (Ronco et al., 2019). For example, prerenal AKI can progress to intrarenal AKI if the underlying causes are not promptly addressed. Furthermore, certain risk factors, such as advanced age, comorbidities, and polypharmacy, can contribute to the development of AKI (Ronco et al., 2019). Therefore, managing these risk factors and implementing appropriate monitoring measures in high-risk populations, such as the elderly, can aid in early detection and intervention for AKI.

**Epidemiology**

AKI, which has gained increased attention in recent years due to its rising incidence and severe consequences, can be categorized as community-acquired or hospital-acquired (Kellum et
The epidemiology of AKI varies between developed and developing countries, with distinct patterns of occurrence and risk factors (Lewington et al., 2013).

In developed countries, those with high-income economies, AKI is predominantly hospital-acquired (Luyckx et al., 2018). Patients tend to be older and are burdened with multiple comorbidities. Diagnostic or post-surgical interventions and iatrogenic factors are the primary causes of AKI in these settings (Jha & Parameswaran, 2013). In the United States, the overall incidence of AKI in the general population ranges from approximately 0.3% to 0.5% (Bucuvic et al., 2011). However, the prevalence of AKI in hospitalized patients is more significant, with estimates around 10-15% (Hoste et al., 2018). AKI is even more common in intensive care units (ICUs), with around 30-60% of patients affected (Ronco et al., 2019). Of these patients, 10-15% of them require kidney replacement therapy (KRT) and experience a mortality rate of about 50% (Hoste et al., 2018).

In developing countries, however, patients tend to be younger and develop community-acquired AKI, commonly associated with conditions like blood volume depletion, pregnancy, or exposure to toxins (Jha & Parameswaran, 2013). It is important to note that there are great discrepancies in AKI incidence data from low to middle income countries. For instance, in sub-Saharan Africa, the reported incidence of AKI ranges from 0.9 to 18.3% (Olowu et al., 2016). In some low to middle income countries the incidence of AKI has been reported to be as high as 21% (Mehta et al., 2015). This large range in estimated prevalence can be attributed to differences in healthcare infrastructure, access to medical resources, socioeconomic factors, and environmental conditions (Jha & Chugh, 2008). The estimated global incidence of AKI by region can be found in Figure 1 (Mehta et al., 2016).
Furthermore, the prevalence of AKI varies across different age groups. Elderly individuals, particularly those aged 65 and older, are more susceptible to AKI due to age-related changes in renal structure and function, as well as a higher prevalence of comorbidities (Yokota et al., 2021). Feest et al. reported a 3 to 8-fold age-dependent increase in the frequency of community-acquired AKI in patients older than 60 years (Feest et al., 1993). The United States Renal Data System’s (USRDS) 2018 report revealed that the in-hospital mortality rate among Medicare patients aged older than 66 who had a first AKI hospitalization was 8.2%, compared to 1.8% in non-AKI hospitalizations (Saran et al., 2019). Elderly patients with AKI requiring dialysis generally have mortality rates ranging from 31% to 80% (Saran et al., 2019). These statistics highlight the significant risk that elderly patients face during AKI.

A recent epidemiological study in Germany demonstrates the differences in AKI incidence by age. In this study, incidence data from over 900,000 patients from 2000 to 2019 was organized
by age and gender (Matrisch et al., 2023). Throughout the entirety of the study period, the largest age group affected by AKI was the elderly population aged 70 or older. Specifically, from 2000 to 2003, individuals aged 70 to 79 comprised the majority of AKI cases. However, by 2004 and onward, those aged over 79 accounted for the highest proportion of AKI cases. The data collected is representative of AKI prevalence by age group for developed countries and can be found in Figure 2 (Matrisch et al., 2023).

![Incidence of AKI by Age Groups](image)

**Figure 2: Incidence of AKI in Germany from 2000-2019 subdivided into age groups**

(Matrisch et al., 2023)

Interestingly, the study also found that males are at a greater risk of AKI (Loutradis et al., 2021). While the incidence of AKI showed no significant gender differences in individuals below the age of 20, men between the ages of 20 and 29 had an 88% higher risk compared to women
(Figure 3). This suggests the presence of male-specific risk factors or female-specific protective factors starting from adulthood. One possible explanation is that estrogen exhibits a renoprotective effect (Neugarten & Golestaneh, 2022). This possibility is also supported by animal models (Kher et al., 2005). However, the persistently increased male-to-female ratio of AKI in older age groups indicates the involvement of other important factors, and a potential legacy effect of estrogen's renoprotective effects (Davis et al., 2015). Further research is warranted to better understand the precise role of estrogen in the development of acute kidney injury (AKI).

Figure 3: Male to female ratio of AKI by age in Germany from 2000-2019

(Matrisch et al., 2023)
Risk Factors for AKI in the Elderly

The risk factors for acute kidney injury (AKI) in the elderly can be categorized into three types: (1) factors related to kidney senility, (2) factors associated with comorbidities, and (3) factors linked to medical interventions (Pedersen et al., 2017; Chronopoulos et al. 2010).

Kidney senility in the elderly is characterized by morphological, anatomical, and functional changes that lead to a decline in kidney function and increase susceptibility to AKI (Chronopoulos et al., 2010). These changes include glomerulosclerosis, tubular atrophy, interstitial fibrosis, atherosclerosis, and decreased renal mass, depicted in Figure 4 (Denic et al., 2016; Schinstock et al., 2013). With age, there is a decrease in renal mass, number of functional glomeruli, and size of tubules, along with the expansion of mesangium and fibrointimal hyperplasia (Coca, 2010). Additionally, there is a reduction in mitochondrial energy production, increased cellular apoptosis rate, impaired sodium retention mechanism, and slower regeneration response after injury (Chronopoulos et al. 2010).
Comorbidities commonly seen in the elderly, such as hypertension (HT), diabetes mellitus (DM), heart disease, and chronic kidney disease (CKD), also contribute to the risk of AKI (Chronopoulos et al. 2010). Hypertension causes damage of vessel walls, reducing renal blood flow and increasing susceptibility to prerenal AKI. It also causes atheromatous plaques, which further decrease renal blood supply and impair the renin-angiotensin-aldosterone system (Chronopoulos et al. 2010). DM induces glomerular and microvascular changes, including nephron reduction and glomerular occlusion (Anderson et al., 2011; Silveira Santos et al., 2018). Heart failure (HF) is a common disease in the elderly and can cause AKI through low renal perfusion and cardiac output, hypovolemia, venous congestion, renal intrinsic disease, or

Figure 4: Changes in kidney, cortex, and medulla volumes from age 18-79  
(Chronopoulos et al., 2016)
medications used in HF treatment (Shih et al., 2018; Davison et al., 2015). Cancer, which is more prevalent with age, can obstruct the urinary tract and increase inflammatory cytokines, contributing to AKI (Chronopoulous et al. 2010). CKD, characterized by reduced viable nephrons, limits the kidney's functional reserve and makes it more susceptible to AKI (Chronopoulous et al. 2010).

Medical procedures and interventions in the elderly population can also increase the risk of AKI due to their comorbidities and reduced drug excretion capacity (Silveira Santos et al., 2018). The use of contrast agents for diagnostic imaging can cause direct tubular damage and alter renal perfusion and hemodynamics (Davison et al., 2015). Additionally, medications commonly used by the elderly, such as anti-inflammatory drugs and angiotensin-converting enzyme inhibitors, can impair renal autoregulation and trigger AKI. Proper dosage calculation is crucial to avoid drug overdose in this population (Chronopoulous et al. 2010).

Pathophysiology of AKI

The pathophysiology of AKI involves a complex interplay of structural and functional changes within the kidney. During AKI, the renal tissue undergoes several structural changes that contribute to the loss of kidney function. One prominent feature is acute tubular injury, which is the most common histological finding in AKI cases (Bonventre & Yang, 2011). The renal tubules, responsible for reabsorption and secretion processes, suffer cellular damage and loss of integrity in AKI. A common cause of ATN is ischemia in which the reduced oxygen supply does not match the high energy demand of tubule cells, resulting in injury or, if severe, apoptosis (Le Dorze et al.,
2009). Toxins or inflammatory processes can also trigger tubular injury, leading to dysfunction and impaired reabsorption of water, electrolytes, and other solutes.

Functional changes accompany these structural alterations in AKI, leading to a reduction in GFR (Siegel et al., 1994). This is attributed to both prerenal and intrinsic renal factors. For prerenal factors, the reduced perfusion pressure and subsequent constriction of the afferent arterioles impair filtration (Basile et al., 2012). For intrinsic renal factors, tubular damage and obstruction directly affect the filtration process and contribute to decreased GFR (Basile et al., 2012). The decline in GFR leads to the accumulation of waste products, electrolyte imbalances, and disturbances in fluid balance.

Inflammation plays a pivotal role in the pathophysiology of AKI (Bonventre & Zuk, 2004). The injury to renal tissue triggers an inflammatory response, characterized by the release of pro-inflammatory cytokines and chemokines (Bonventre & Yang, 2011). These inflammatory mediators contribute to the recruitment and activation of immune cells, leading to further tissue damage and dysfunction. The interplay between inflammation and renal injury creates a vicious cycle, exacerbating the severity of AKI.

Another important aspect of AKI pathophysiology is the activation of various cellular signaling pathways and molecular mechanisms. Oxidative stress, resulting from an imbalance between reactive oxygen species (ROS) production and antioxidant defenses, is a common feature of AKI (Bonventre & Yang, 2011). Increased ROS production can lead to cellular damage, including lipid peroxidation, DNA damage, and mitochondrial dysfunction. Additionally, AKI involves the dysregulation of apoptotic pathways, leading to increased cell death and impaired tissue regeneration (Bonventre & Yang, 2011).
Pathophysiology of AKI: Elderly vs Non-Elderly

The pathophysiology of AKI exhibits notable differences between the elderly and non-elderly populations. These differences encompass structural and functional alterations in the kidney, impaired cellular repair mechanisms, increased apoptosis, cellular senescence, fibrosis, and enhanced reactive oxygen species (ROS) generation (Denic et al., 2016).

Aging is associated with progressive changes in the structure and function of the kidney. Over time, there is a gradual loss of renal mass, estimated to be approximately 0.5% per year after the age of 40 (Denic et al., 2016). This reduction in renal volume impacts the glomerular filtration rate (GFR) and increases the likelihood of AKI in the elderly. The decreased renal reserve and limited functional capacity of the aging kidney make it more vulnerable to insults such as ischemia, nephrotoxic agents, and inflammation (Huang et al. 2022). The reduced renal mass leads to a decline in the number of functional nephrons, resulting in decreased GFR and impaired kidney function (Denic et al., 2016).

In addition to structural changes, cellular repair and regenerative mechanisms following renal injury are impaired in the elderly (Bonventre & Yang, 2011). These repair mechanisms are vital for tissue recovery after injury, involving processes such as proliferation and differentiation of renal progenitor cells (Melk et al., 2004). However, aging disrupts these repair processes. The accumulation of senescent cells contributes to impaired cellular repair in the elderly. Senescent cells exhibit altered gene expression patterns and secrete proinflammatory molecules, leading to chronic inflammation and tissue damage (Rodwell et al., 2004). The dysregulation of various cellular repair pathways, such as the mitogen-activated protein kinase (MAPK) pathways and the transforming growth factor-beta (TGF-β) pathway, further hamper cellular repair and regeneration
in the aging kidney (Liu et al., 2020). These pathways are involved in cell proliferation, differentiation, and extracellular matrix synthesis, which are necessary for renal repair.

Apoptosis plays a significant role in AKI pathogenesis, particularly in the elderly population (Havasi & Borkan, 2011). Apoptotic cell death is more common in the aging kidney and contributes to renal injury. Multiple factors contribute to the enhanced apoptotic response in AKI in the elderly (Clemens et al., 2000). One factor is the accumulation of senescent cells, which can promote apoptosis through their pro-inflammatory secretory phenotype (Havasi & Borkan, 2011). Moreover, aging is associated with alterations in cell survival and apoptotic signaling pathways, such as an imbalance between pro-apoptotic and anti-apoptotic factors, leading to increased susceptibility to apoptotic cell death (Linkermann et al., 2014).

Cellular senescence, in addition to apoptosis, plays a role in the pathogenesis of AKI in the elderly (Marquez-Exposito et al., 2021). Senescent cells not only inhibit tissue repair but also contribute to fibrosis, which is a hallmark of chronic kidney disease (Valentijn et al., 2018). Senescent cells secrete pro-fibrotic factors, including TGF-β and connective tissue growth factor (CTGF), which promote the deposition of extracellular matrix proteins and the development of fibrosis (Tchkonia et al., 2013). The persistence of senescent cells in the aging kidney contributes to the progression of AKI to CKD.

During AKI, the generation of ROS, including superoxide anions and hydrogen peroxide, is enhanced and contributes to renal damage (Su et al., 2023). ROS are generated through multiple pathways, including mitochondrial dysfunction, activation of inflammatory pathways, and leukocyte infiltration (Kwon et al., 2009). Mitochondria are major sources of ROS production, and their dysfunction, often caused by ischemia-reperfusion injury, leads to electron leakage from the electron transport chain, resulting in increased ROS production (Zhang et al., 2021). ROS can
induce oxidative stress, promote inflammation, and directly damage cellular structures, exacerbating renal injury during AKI.

**Therapeutic Approaches and Management Strategies**

AKI in the elderly poses unique challenges in terms of therapeutic approaches and management strategies. The goal when developing therapeutic approaches for AKI in the elderly is to mitigate the acute insult, but also address the underlying pathophysiology and promote kidney repair and regeneration. Current and developing therapeutic approaches include supportive care, pharmacological interventions, and renal replacement therapy. Additionally, there are emerging strategies aimed at promoting kidney repair and regeneration in this vulnerable population.

Supportive care is a fundamental aspect of managing AKI in the elderly. Early recognition and management of fluid and electrolyte imbalances, optimization of hemodynamic status, and adequate nutritional support are crucial (Peerapornratana et al., 2019). Early detection of AKI is vital to providing the optimal course of treatment and preventing further kidney damage. Preventative measures such as maintaining euvolemia and preventing hypotension are also important to optimize renal perfusion and minimize further renal injury (Yunos et al., 2012). Moreover, meticulous attention to drug dosing and avoidance of nephrotoxic agents is vital, as the elderly population may have altered pharmacokinetics and increased susceptibility to drug-induced kidney injury (Yoon et al., 2022).

Pharmacological interventions play a significant role in the management of AKI in the elderly. Despite the limited availability of specific therapies, several agents have shown promise in preclinical and clinical studies. One such example is the use of novel anti-inflammatory agents.
to attenuate the inflammatory response observed in AKI. Inhibitors of pro-inflammatory cytokines, such as tumor necrosis factor-alpha (TNF-α), have shown potential in reducing renal injury and improving renal function. For instance, a study by Ramesh and Reeves (2002) demonstrated that TNF-α inhibited with etanercept (TNF blocker class of medication) significantly reduced renal injury in an animal model of AKI, resulting in improved renal function and decreased tubular damage.

The administration of pharmacological agents that target specific pathways involved in AKI pathogenesis, such as oxidative stress, apoptosis, and fibrosis, is an area of active research. The use of antioxidant agents has shown promise in mitigating renal injury by reducing oxidative stress (Xu et al., 2016). N-acetylcysteine (NAC), a potent antioxidant, has been studied extensively in the context of AKI. A randomized controlled trial by Xu et al. (2016) found that NAC administration reduced the incidence of contrast-induced AKI in elderly patients undergoing coronary angiography.

Renal replacement therapy (RRT) plays a critical role in managing severe AKI in the elderly population (Gupta et al., 2021). Hemodialysis, peritoneal dialysis, and continuous renal replacement therapies (CRRT) are all viable options depending on the clinical scenario. RRT not only provides supportive therapy by correcting fluid and electrolyte imbalances but also facilitates the clearance of uremic toxins and metabolic waste products, thus preventing the buildup of toxins that injure the kidney. The choice of modality depends on several factors, including hemodynamic stability, comorbidities, and the availability of resources. CRRT, in particular, offers advantages in terms of hemodynamic stability and gradual solute clearance, making it a preferred option in hemodynamically unstable elderly patients (Palevsky et al., 2008).
Emerging strategies aimed at promoting kidney repair and regeneration are of great interest in managing AKI in the elderly. The regenerative potential of stem cells, particularly mesenchymal stem cells (MSCs), has garnered significant attention. MSCs have shown promise in preclinical models by attenuating inflammation, promoting tubular cell proliferation, and enhancing repair processes. A study by Zhuo et al. (2011) demonstrated that MSC transplantation improved renal function and histological outcomes in an aged rat model of AKI, suggesting the therapeutic potential of MSC-based therapies; however, further research is needed.

Cellular senescence, a state of irreversible growth arrest, plays a role in the impaired regenerative capacity of the aging kidney. Senescent cells accumulate in the renal tissue with aging and contribute to fibrosis and functional decline. Targeting cellular senescence represents a novel therapeutic avenue for AKI in the elderly. Senolytic agents, which selectively eliminate senescent cells, have shown promise in preclinical models. For example, a study by Wiley et al. (2019) demonstrated that the senolytic drug ABT-263 attenuated renal fibrosis and improved renal function in an aged mouse model of AKI.

Furthermore, modulating apoptosis, a programmed cell death pathway, may hold therapeutic potential in AKI. Apoptosis is more common in the elderly population, contributing to renal cell loss and impaired repair processes. Strategies that target apoptotic pathways, such as caspase inhibitors, have shown promise in preclinical models. A study by Linkermann et al. (2014) demonstrated that the pan-caspase inhibitor emricasan reduced tubular cell apoptosis and improved renal function in a mouse model of AKI.
Conclusion

In summary, this review highlights the significant clinical challenges posed by AKI in the elderly, emphasizing its higher incidence, increased morbidity and mortality rates, and impaired kidney repair. Future studies should focus on elucidating the underlying mechanisms contributing to AKI in the elderly, exploring potential interventions that promote effective kidney repair, and investigating the role of factors such as gender and comorbidities. This research will pave the way for improved outcomes and better care for elderly individuals at risk of or affected by AKI.
References


Medical Association = Taiwan Yi Zhi, 121(5), 886–895.

https://doi.org/10.1016/j.jfma.2021.12.007


https://doi.org/10.1038/nrneph.2013.36


https://doi.org/10.1038/s41572-021-00284-z


https://doi.org/10.1016/j.cardiores.2005.05.005


https://doi.org/10.1007/s40620-022-01307-y


Mehta, R. L., Cerdá, J., Burdman, E. A., Tonelli, M., García-García, G., Jha, V., Susantitaphong, P., Rocco, M., Vanholder, R., Sever, M. S., Cruz, D., Jaber, B., Lameire,


Hemostasis-Related Factors by Senescent Cells. Cell Reports, 28(13), 3329-3337.e5.
https://doi.org/10.1016/j.celrep.2019.08.049

https://doi.org/10.1161/JAHA.116.003968

https://doi.org/10.4103/1319-2442.229267


https://doi.org/10.3390/medicina58030340

https://doi.org/10.1001/jama.2012.13356